THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

AUGUST, 1927

ORIGINAL ARTICLES.

COCCIDIOIDAL GRANULOMA.

I. Review of the Clinical Data with Report of a Pennsylvania Case.

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and

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Coccidioidal granuloma is a disease that must be differentiated from tuberculosis, blastomycosis and various lymphatic diseases. The diagnosis, in any case, must rest upon the isolation of the organism in culture and in tissue. The geographical distribution in this country is rather limited, the majority of cases having appeared in California. The present case is the first one to be reported in Pennsylvania.

Case Report. The patient, an American boy aged five years, who had lived in the east all his life with the exception of a two-months visit to New Mexico, was placed under the care of one of us (D. R.) because of a long-continued low fever. Aside from hayfever and asthma affecting two members of the family, there were no other chronic familial diseases that would have a bearing on this illness.

The boy was perfectly healthy until the end of the fourth year when (in March, 1923) he had what was considered to be intestinal influenza. This was characterized by intermittent diarrhea,

weakness, pain and fever. This illness lasted three months and was followed by a persistent night cough and slight fever. From that date on, the posterior cervical and right axillary lymph nodes were enlarged. In September, 1923, the cough became worse and the fever increased. At this time a diagnosis of pneumonia was made. After recovery from this acute illness, he had a bilateral otitis media necessitating puncture of both ear drums. The temperature then became normal and remained so until November, 1923, when he had a severe cold, possibly a bronchopneumonia, the acute symptoms lasting two weeks. The tonsils and adenoids were removed late in November, 1923. In spite of a gain of 2 or 3 pounds in weight and contrary to expectations, another febrile cold set in about Christmas and persisted up to the time the boy came under observation in January, 1924.

At this time the physical examination showed a large head, rather deep set eyes, with dark circles beneath. The tongue was slightly coated; the teeth in fair condition. There was no tenderness over the mastoid area. On the right side of the neck there was a mass of enlarged glands. Another gland, the size of a large walnut was found at the inner end of the left clavicle, and above this a smaller gland. Posteriorly, one or two were found below the hairline on the left side, outside the border of the trapezius muscle. The right sternoclavicular joint was unduly prominent. The heart showed sinus arrhythmia. At the apex of the left lung the breath sounds were harsh but there were no râles. The spleen was not palpable. The liver extended from the fifth interspace to a little beyond the costal border. The knee jerks were present; there was no Babinski reflex; the plantar reflex was active.

Further Course. January 22, 1924: The patient is about the same. The temperature during the interval has ranged from 99° to 100.4° F., and was distinctly higher on rainy days. Cough occurs only at nights. There has been one slight nosebleed. Some engorged veins are visible on the upper chest; the tactile fremitus is diminished over the left upper lobe. No particular change in respiratory sounds is noticeable but a few râles are heard at the left apex.

January 25: On this day a cervical gland was excised at the University Hospital by Dr. E. L. Eliason, and the specimen sent to Dr. Herbert Fox for diagnosis.

February 25: Since the previous examination the temperature has continued to be hectic ranging from 102° to 103° F. in the afternoons and being normal or nearly so in the mornings. The cough has been more persistent and has become brassy. Wheezes are sometimes heard at night. The patient appears more tired. A fluctuating point has developed under the cervical scar. The mass of glands in the neck has grown to the size of half an apple.

There is no undue venous engorgment. The breath sounds are a little rough. The liver and spleen are not enlarged.

March 8: The patient is distinctly worse and has pain in the left groin and the right chest. He is restless and not eating well. Two swellings have developed on the scalp. The glands in the neck do not appear so large but on percussion the mediastinal glands seem large. In the left pleural sac there is apparently an effusion.

April 8: The patient lies constantly on the left side; breathing is rapid. There is considerable abdominal pain and distention. The abscess on the top of the head is discharging a viscid light brown material. The upper chest is dull on both sides. Posteriorly, over the middle of the left chest there is a large, soft, not tender, fluctuating swelling. The breath sounds over the left chest are bronchial; the tactile fremitus greatly diminished.

April 13: The condition is no better. There is a great deal of abdominal distention.

April 17: After tapping the left chest the child seemed better for a day or two, then he became more distressed than before. The cough is hard and croupy. The left chest has filled again with fluid. Posteriorly there are three or four separate masses, the largest being the size of a hen's egg. All of these fluctuate. The abdomen is greatly distended, the liver large and depressed. Across the upper chest, extending from the sternum nearly to the shoulder on the left and not quite so far on the right, is an area of dullness over which the breath sounds are harsh but not bronchial. The reflexes are normal.

May 1: Dr. Eliason operated on the patient for multiple abscesses, one in the scalp, one in the neck beneath the scar of the cervical adenectomy, and one located on the left chest posteriorly. Local anesthesia was used. The same type of viscid "café-au-lait" pus was found.

May 2: The patient who had grown steadily weaker died today.

During the course of the illness arsenical remedies and iodids were administered with no relief. Alpine light was used by Dr. Percival Nicholson and was also without any alleviating effect.

Laboratory Findings. *Blood Count.* January 11, 1924: Hemoglobin, 82 per cent; red blood cells, 3,260,000; white blood cells, 9080; polymorphonuclears, 61; lymphocytes, 36; large mononuclears, 2; transitionals, 1. January 26: Hemoglobin, 70 per cent; red blood cells, 4,650,000; white blood cells, 22,800; polymorphonuclears, 70; lymphocytes, 7; large mononuclears, 6; transitionals, 3; eosinophils, 12; basophils, 2.

Coagulation Time. January 25, 1924; nine and five-tenths minutes.

Urinalysis. Occasionally there was a faint trace of albumin but no other abnormal finding.

Fractional Gastric Analysis. No lactic acid or occult blood was found.

Fasting.	Free HCl.	Total acid.
1	46	67
2	47	67
3	26	64
4	22	54
5	27	60

Roentgen ray, by Dr. Henry K. Pancoast.

January 18: "The lungs are negative. There is a very extensive glandular enlargement or neoplasm involving the mediastinal space."

February 26: "The mediastinal shadow has increased considerably since the previous examination."

Biopsy. Microscopic examination of a cervical gland was made by Dr. Herbert Fox. "Section of gland shows a chronic inflammatory process. It is tuberculous in the sense that there are areas of granulation tissue with many giant cells. Three structures resembling oïdiomyces were found in the giant cells. The histology is comparable to that described for blastomycosis or oïdiomycosis."

February 12: "Further study has revealed many of the forms described in the first report, including one showing internal sporulation but none showing budding or growth into mycelia."

Diagnosis. Coccidioidal granuloma.

Bacteriologic Report. Smears from the nodules on the scalp and from the chest fluid showed the typical organism and produced growth on culture.

Cultural Studies. Cultural studies of the organism as determined by growth on various media gave the following results:

Glucose agar, 2 per cent; acid, 1 per cent. A white fluffy growth is visible on the second day. Aërial hyphæ are produced, which give the surface the appearance of whiteness of dry snow. The hyphæ penetrate into the medium. About the fifth day the edge of the medium becomes discolored and of a brownish tinge.

Potato: There is abundant growth and a brownish discoloration at the edge of the medium on the fifth day.

Sugars: No fermentation.

Broth: Good growth. On the third day a membrane is formed over the top and flakes are seen in the broth.

Hanging drop: From the broth culture a hanging drop shows branching hyphæ, or mycelia, which eventually form an intricate meshwork. At the ends of the mycelia are seen club-shaped forms. No spores are seen nor is there any budding.

The Organism in Tissue. The form is distinctly spherical, 15 to 40 μ in diameter. It has a double-contoured membrane or capsule which contains granular, or vacuolated, or segmented protoplasm. Between the protoplasm and the capsule there is an area which

does not take the stain. At times one sees the spherical bodies filled with spores. Budding has never been seen. The organism stains well with the following stains: Delafield's hematoxylin-eosin, methylene blue and eosin, Gram's and iron-hematoxylin.

Animal Experimentation. The disease was successfully reproduced in guinea pigs and rabbits by intravenous, intraperitoneal, and subcutaneous inoculations. Pin point nodules were found in the lungs, spleen, liver and testicles. The typical organisms were seen in the tissue sections and were recovered in cultures from various organs. Therefore, the bacteriologic and pathologic findings establish the diagnosis of coccidioidal granuloma. A fuller report of the study in animals will be published in a succeeding paper.

Review of the Clinical Literature. We were able to find reports of 87 cases. It is a striking fact that the majority of the cases have occurred in inhabitants of California or in persons who had previously lived in that state, and especially in the San Joaquin Valley. Of a total of 78 cases, where the residence was stated, 70 occurred in California, and of these 19 were from the San Joaquin Valley and 51 from the remainder of the state.

The disease seems to affect chiefly the male sex, only 6 of the 87 cases occurring in females. Race appears to play no part. As to the occupation we find that 19 were farm laborers, 5 were cattle men, and 5 railroad workers. Single cases have occurred in nearly all trades and professions. In respect to age we find that of 76 cases where the age was known, 41 were between twenty and forty years, and 8 were in children of less than ten years.

Clinical Types of Coccidioidal Granuloma. Clinically there are several types of the disease, yet the distinction is not clearly cut. One type tends to merge into another as the disease spreads throughout the body. Regardless of the type the general symptoms are loss of weight and strength, anorexia, hectic fever, sweating and a tendency to lymphatic involvement. If the lesion is localized and remains superficial the disease may run a very chronic course, even from ten to fourteen years. As soon, however, as the disease becomes systemic the course becomes more acute and is fatal in a few weeks or at the most months. The most common types found are those involving the respiratory tract, the osseous system or the skin. Aside from the general symptoms described, special symptoms pertaining to the particular tissue involved are observed. Skin lesions are often followed by local joint or bone lesions.

In the respiratory type the differential diagnosis must be made from pulmonary tuberculosis, pneumonia and empyema. The osseous type might easily be confused with bone tuberculosis, osteomyelitis, and arthritis. The skin lesions simulate lupus vulgaris, blastomycosis, actinomycosis, sporotrichosis and septicopyemia.

In rare instances the initial lesion is found in the central nervous system, the gastrointestinal tract or in the lymphatic system. When the nervous system is involved the differential diagnosis must be made from tuberculous meningitis and epidemic meningitis. In the gastrointestinal type typhoid fever must be ruled out. The lymphatic type must be differentiated from lymphatic leukemia, Hodgkin's disease and lymphosarcoma. The final diagnosis rests entirely on the discovery of the organism both in culture and in tissue.

Differential Diagnosis. The points to be stressed in the differential diagnosis from blastomycosis are: In coccidioidal granuloma the skin lesions are generally secondary, while in blastomycosis they are generally primary. Blastomycosis tends to remain chronic and is considerably relieved by large doses of potassium iodid. Blastomycosis may sometimes become generalized and there are several instances reported in which the meninges were involved. Just as coccidioidal disease is most common in California, so blastomycosis occurs most frequently in and about Chicago. It is possible that a greater local interest in the disease accounts for this. Blastomycosis is apparently carried only by the blood stream while coccidioidal granuloma may spread both by the blood and the lymph channels. In blastomycosis budding is seen both in cultures and in the smears from the affected tissues.

Coccidioidal granuloma, blastomycosis, as well as the other fungoid diseases, should be thought of: (1) If the sputum in a case of chronic pulmonary disease does not show tubercle bacilli on repeated examinations; (2) if the patient has lived on the Pacific slope.

In all pulmonary cases not typically or definitely tuberculous, the sputum should be cultured on various media, especially glucose agar, for other organisms than the tubercle bacilli, for the coccidioides, the streptothrix and other fungi and yeasts.

Whenever the lymph nodes are enlarged in typical cases a gland should be removed for biopsy; part of it should be used for culture and part fixed for staining. With the free intercourse that obtains in this country among the citizens of all the states, it is improbable that blastomycosis is limited to the environs of Chicago and coccidioidal granuloma to the San Joaquin Valley of California.

Treatment. No drug that has been used thus far has been of any help. Roentgen ray exposure is thought to have relieved some of the bone lesions, especially if the treatment was applied after amputation. The only real cure occurred in cases in which the lesion had been entirely excised while it was local. No generalized case has ever recovered. Of the reported cases, 11 have been benefited by surgery.

Abstract of Cases from the Literature. CASE I.—Wernicke (1892). The lesions consisted of nodules in the skin which disfigured the nose and the

cheek. There were masses in the left groin, in the calf and the buttock. Wernicke described the organism he found in the granulation tissue and lying free "light yellow masses with a glistening shell." These bodies seemed to have granular or globoid interior but not a distinct nucleus. When fixed the interior was not filled out to the capsule. Some contained daughter cysts.

Case II.—Gilchrist and Rixford (1896). A male, aged forty years, a manual laborer on trams and about docks in San Francisco and a native of Fayal in the Azores; he came to California in 1886. The skin lesions on the back of his neck and on his forehand first appeared in 1885. He came to the hospital in 1893 and at that time the lesions had extended to both upper eyelids, the nose, cheeks, lips, left ear and dorsum of the right hand at the base of the index finger. It is interesting to note that the mucous membrane of the mouth, nose and conjunctiva were more resistant. The disease entered the orbits without apparently affecting the conjunctiva. In February, 1894, the lymph glands of the neck began to swell and fluctuate. The temperature became intermittent. The patient developed a cough which became steadily worse. The left tibia became involved and the left testicle became abscessed. It was thought that the patient had contracted tuberculosis. The duration was nine years. Upon autopsy, lesions were found in the skin, lungs, diaphragm, peritoneum, spleen and lymph glands. Gilchrist described the organism and called it a protozoan. Cultures were not successful but some of the animal inoculations were.

Case III.—Rixford and Thorne (1894). A male, Portuguese, aged thirty-three years, laborer and saloon keeper, who had lived in California for fourteen years, chiefly in the San Joaquin Valley. On June 1, 1894, the patient had hematemesis and complained of weakness. About five weeks later he observed blood in the urine and some reddish spots on his forehead, left arm and breast. The eruption was painful. The patient entered the hospital in August. The cervical and inguinal glands became involved. The duration was one month. There was no autopsy but the biopsy showed the characteristic organism. Animal inoculation was successful. There is no report in regard to the culture.

Case IV.—Ophüls and Moffitt (1900). A male, aged nineteen years, farm laborer, born in the Azores, entered the hospital, January 26, 1900. The symptoms began in December 1899, with a chill. A few days later the left pleura was tapped and 1 gallon of clear fluid was withdrawn. The temperature became irregular. The joints became involved. The cervical glands became enlarged and tender. The patient developed a cough with sanguinous sputum. He died, February, 1900 (two months duration) with a diagnosis of septicopyemia. The autopsy showed lesions in the lungs, diaphragm, lymph glands, spleen, kidney, liver and bone. The characteristic microscopic and cultural findings were obtained.

Case V.—Montgomery (1900). A male, German, aged twenty-one years, telegraph operator, came to California at the age of three years. The symptoms began with cough in July, 1898. He came to the hospital in April, 1899, with a diagnosis of pulmonary tuberculosis. The patient had skin lesions, two on the scalp, eight on the face and two on the forearm. The cervical lymph glands became enlarged. He suffered from weakness, night sweats and loss of weight. The duration was ten months. Autopsy showed lesions in the lung, liver and in the skin. The characteristic microscopic and cultural findings were obtained. Animal inoculations were not successful.

CASE VI.—Montgomery, Ryfkogel and Marrow (1903). A man, a native of Switzerland, aged fifty-four years, who worked on the ranches and as a miner, came to California at the age of seven years. In 1895 he noticed a gradual enlargement of his left hand and forearm. In 1896 the left leg and ankle began to swell. In 1899 an eruption appeared on his chest. In 1900 the eruption had spread to the left forearm, hand, neck and ears. His general health was good until December 15, 1901, when he became weak, had anorexia and pain in the temporal region. The duration was six years. Autopsy showed lesions in the lungs and in the skin. The characteristic microscopic and cultural findings were obtained. Animal inoculations were successful.

CASE VII.—Gardner (1904). A man, aged thirty-two years, Swede, worked on a ranch at Newman, came to California in 1895. The symptoms began in 1900, when the patient sprained his right ankle. The foot became swollen and painful, and an abscess developed on the dorsum of the foot. The abscess was opened and considerable necrosed bone and pale granulation tissue was removed. The lymphatic glands in the right groin became enlarged. The foot was amputated and the inguinal glands were removed. The characteristic microscopic and cultural findings were obtained.

CASE VIII.—Wolbach (1904). A female, age not stated, who had lived in Mexico and California. The patient complained of eczema with intense itching, frequent boils and chronic nasal catarrh. In 1903 she had two swellings on her head, forehead and mastoid process extending through the bone and stopping at the dura. The sores were curetted and cleaned. The characteristic microscopic and cultural findings were obtained.

CASE IX.—Ophüls (1905). A man, German, age not stated; occupation not stated, was admitted to the hospital, May 8, 1900, in an unconscious condition. He was breathing stertorously. There was a slight paresis of the muscles of the right side of the face. The extremities were rigid. There was no other paralysis. The duration was five days. Autopsy showed that the pia mater at basis of the brain and in the Sylvian fissure was diffusely infiltrated with pus and submiliary yellow nodules. There was a little turbid fluid in both ventricles. The characteristic microscopic and cultural findings were obtained.

CASE X.—Ophüls (1905). A male, Japanese, age not stated, was employed by Santa Fé Railroad. He had a chronic ulcer of the right foot just below the ankle. The femoral and the inguinal lymph glands became involved. The diagnosis was made through biopsy.

CASE XI.—Ophüls (1905). A man, aged nineteen years, a canner, had been in San Joaquin Valley for twelve years and one month before he came to the hospital in September 23, 1901. Four weeks previous to his entering the hospital he had attacks of irregular fever with violent chills. The patient developed the symptoms of a severe, unusually chronic meningitis, and had much headache, marked rigidity of the neck, tenderness of the cervical vertebra and constipation. The duration was three months. The autopsy showed lesions in the lung, kidney and adrenal; also, basilar meningitis with many tubercles in the Sylvian fissures and very extensive chronic inflammation of the pia mater of the spinal cord. The characteristic microscopic findings were obtained. There was no report on the culture.

CASE XII.—Ophüls (1905). A German, aged sixty-three years, worked as a baker and as a mill hand in Oakland and Sacramento. He came

to the hospital with enlarged, suppurating cervical glands. In 1903 he developed a "cold" abscess in the left side of the chest. This abscess was opened and two ribs were resected in March, 1904. The wound never closed. The sinus was curetted and some of the diseased bone was removed. The characteristic microscopic and cultural findings were obtained.

Case XIII.—Ophüls (1905). A male, Chinese, age and occupation not given, who had lived in San Francisco. In June, 1905, the external condyle of the right humerus was resected on account of caries, which involved the elbow joint. The patient died in a short time. Autopsy was not permitted but the microscopic findings were characteristic.

Case XIV.—Brown (1907). A male, aged twenty-five years, Japanese, was a laborer of the South Pacific Company at Bakersfield. It was thought that he had beriberi. In November, 1905, he became ill with fever, cough and pain in the chest. Several of the joints were involved. The glands became affected. The patient died, January, 1906. Autopsy showed abscesses in various parts of the body, lesions in the lungs, spleen and mesenteric glands. The characteristic microscopic and cultural findings were obtained.

Case XV.—Brown (1907). A man, aged twenty-eight years, who irrigated ditches near Fresno, was admitted to the hospital with general malaise. He had an ulcer on the left wrist, several swellings in the neck and on the seventh, eighth and ninth ribs in left parasternal line. The disease was fatal. Autopsy showed the lungs studded with miliary tubercles. The characteristic microscopic and cultural findings were obtained.

Case XVI.—Brown (1907). A Japanese, aged twenty-eight years, worked for the Southern Pacific Railroad as a track worker. He complained of pain in the ankle joint with swelling and developed cervical adenitis. The characteristic microscopic and cultural findings were obtained.

Case XVII.—Brown (1907). A male, aged twenty-four years, Greek; occupation was not stated. He lived eighteen months in San Joaquin Valley. The symptoms began June, 1906, with pain in the left axilla. Pustules then appeared on the forehead and scalp, and a cough developed. There were no cultural examinations, but the microscopic findings were characteristic.

Case XVIII.—Ryfkogel (1912). A Japanese, aged thirty years, a teamster in San Joaquin Valley. He was treated for typhoid fever in January, 1911. A swelling in the right heel and tenderness in the left shoulder and hip developed. The duration was three months. The characteristic microscopic and cultural findings were obtained.

Case XIX.—Carson and Cummins (1913). A male, American, aged twenty-four years, whose occupation was not stated, had lived in the San Joaquin Valley. The illness began with a "cold." His temperature and pulse were of typhoid character. He had severe general headache and diarrhea. Autopsy revealed lesions in spleen, liver, kidney and lungs. The characteristic microscopic findings were obtained. The cultural findings are not reported.

Case XX.—Bowles (1912). A Japanese, aged thirty years, was a farmer and teamster and lived in San Joaquin Valley. He had been

treated for typhoid fever. Tenderness in the right heel, in the shoulder and hip developed. The Roentgen ray showed necrosed bone, which was curetted. The microscopic and cultural findings were characteristic.

CASE XXI.—Brown (1913). A male, aged two years; residence not stated. The symptoms resembled those of tuberculosis. The patient suffered from headache, vomiting, high temperature and double optic atrophy. The disease was fatal. The microscopic and cultural findings were characteristic.

CASE XXII.—Brown (1913). A male, aged twenty years, Indian, was a laborer in a construction gang in San Joaquin Valley. He complained of cough and weakness. Five days after admission he died. Autopsy revealed miliary lesions in the lungs. The culture was not reported. The microscopic findings were characteristic.

CASE XXIII.—Morris (1913). A male, aged thirty-seven years, American, occupation not stated, had lived in Brownwood, Texas. During the winter of 1911–1912 he suffered from a cough. In November, 1912, pain developed in several joints. In January, 1913, it was thought that he had a liver abscess. The weakness continued until he succumbed in May, 1913. The microscopic findings were characteristic.

CASE XXIV.—Chipman (1913). A male, aged twenty-eight years, race not given, machinist, had lived two years in San Joaquin Valley. The lesion began as a pimple on the left side of the nose in August, 1912. The submaxillary lymph nodes were enlarged. The patient suffered from cough and loss of weight. The disease was fatal in three months. The diagnosis was made from the smears.

CASE XXV.—Powers (1914). A man, aged forty-four years; race and occupation not stated. He traveled through the south and in Europe and as early as 1902 noticed nodules in his neck. He spent the winter of 1910 in California and at this time many nodules appeared on neck, chest and abdomen. He died from exhaustion, April, 1912. Autopsy showed miliary abscesses of the liver, spleen and kidney and caries of the thoracic vertebræ. The microscopic and cultural findings were characteristic.

CASE XXVI.—Roblee (1914). A male, full-blooded Indian, aged eighteen years. The patient complained of a sensitive spot and swelling over the outer side of the head of the left tibia. In January, 1914, he developed an irregular temperature. A fluctuating mass developed in the right axilla. Many abscesses developed and the patient died a few months later. The characteristic findings were obtained.

CASE XXVII.—Cooke (1915). A Portuguese, aged twenty-five years, a milker on a ranch near Newman, Calif. In March, 1912, he noticed a painful lump on his right wrist. The right knee became involved and other suppurating foci developed over the right shoulder, left arm, left ankle and beneath the scalp. The patient became considerably emaciated and weak and died March 1914. The microscopic and cultural findings were characteristic.

CASE XXVIII.—Cooke (1915). An Italian, aged twenty-nine years, occupation not stated, came from Bakersfield, Calif. The cervical glands were greatly enlarged and masses developed on his forehead. The patient died on the fourth day after admission, from asphyxiation. Autopsy

showed numerous abscesses filled with yellowish pus. The lungs were bound down by adhesions but there were no gross lesions. The cultural findings were characteristic.

CASE XXIX.—Brown and Cummins (1915). A Mexican, aged twenty-nine years, a laborer in a railroad gang at Bakersfield, Calif., came to the hospital, July, 1913. Three weeks previous to his admission he noticed a nodule on the dorsum of his right great toe. He became emaciated, had a high irregular temperature, became stuporous and died. Autopsy showed lesions in the spleen, kidneys, lungs and a uniform thickening of the occipital dura mater. There was also necrosis of the temporal bone, sternum, third, fourth, and fifth lumbar vertebræ and the bones of the right toe. The microscopic and cultural findings were characteristic.

CASE XXX.—Brown and Cummins (1915). A male, aged twenty-four years, race and occupation not given, had lived in San Joaquin Valley. He came to the hospital in August, 1912, with typhoid symptoms. He died March, 1913. Autopsy revealed apparently a disseminated miliary tuberculosis. Lesions were found in the spleen, lungs, liver, kidney, pancreas and adrenals. The microscopic and cultural findings were characteristic.

CASE XXXI.—Brown and Cummins (1915). A male, aged twenty-seven years, race not given, a blacksmith helper in Kerto, Calif., came to the hospital in March, 1914. The symptoms began with lumbar pain. He lost 13 pounds in fifteen days, and died in three months. The diagnosis was based upon smears.

CASE XXXII.—Dickson (1915). The age, sex, occupation and location were not given. The lesion was in the wrist and knee. The microscopic and cultural findings were characteristic.

CASE XXXIII.—Dickson (1915). A male farm laborer, age not given, who had lived near Colussa, Calif., came to a physician, June, 1908, on account of an abscess between the thumb and index finger. An abscess developed on the side of the face. He developed a cough and died, November, 1910. The microscopic and cultural findings were characteristic.

CASE XXXIV.—Dickson (1915). An Australian sailor, aged thirty-nine years, who had worked as a rope splicer in the oil fields of Kern County in the San Joaquin Valley, he was admitted to the hospital, February 14, 1909. He complained of pain in the chest, had a cough, sweats and lost twenty-two pounds in three weeks. He had pleural effusion, and 2000 cc. of pleural fluid was removed. The cervical glands became enlarged. He died, July, 1910. Autopsy showed lesions in the meninges, lungs, pleura, lymph nodes, liver, spleen, kidneys, ribs and sternum. The microscopic and cultural findings were characteristic.

CASE XXXV.—Dickson (1915). A brakeman on the Southern Pacific Railroad in the San Joaquin Valley was admitted to the hospital, July, 1911, complaining of a stiff and painful elbow. The right elbow was completely ankylosed and there was marked atrophy of the muscles of the arm. The elbow was resected in August. The microscopic findings were characteristic.

CASE XXXVI.—Dickson (1915). A Hindu, aged twenty-six years, occupation and location not stated. He had been treated for a tuberculous knee. His left elbow became stiff and swollen. He died, August,

1912. Autopsy revealed lesions in the lung, pleura, lymph nodes and synovial membrane of the left elbow and lumbar vertebra. The microscopic and cultural findings were characteristic.

CASE XXXVII.—Dickson (1915). A Mexican laborer practically moribund. He had been treated for disseminated miliary tuberculosis. The microscopic findings were characteristic.

CASE XXXVIII.—Dickson (1915). A German, aged fifty-nine years, occupation not given, came to the hospital in July, 1913. He complained of "pain in the bowels" which came on four hours after eating. The diagnosis of duodenal ulcer was made. The characteristic microscopic findings were obtained.

CASE XXXIX.—Dickson (1915). An American, aged sixty-five years, a housewife. She complained of pain in the left ankle, which had persisted for eight weeks. The diagnosis was based upon microscopic findings.

CASE XL.—Dickson (1915). A Jamaican negro, sailor, aged twenty-one years who had lived for four months in Coalinga, Calif. He came to the hospital, January, 1914, complaining of a sore foot. The foot was amputated May 2. During June and July a fluctuating mass appeared on the right side of the chest, on the side of the left leg and in the right arm. The patient left the hospital. The microscopic and cultural findings were characteristic.

CASE XLI.—Lipsitz, Dawson and Fessenden (1916). A colored sleeping-car porter, aged twenty-eight years. He lived in Kentucky but traveled from St. Louis to Denver, never any further west. He came to the hospital in July, 1915. The illness began three weeks previous with coryza, hoarseness and cough. He lost 10 pounds in three weeks. On July 1 painful nodules developed in the calves of his legs. In ten days, 13 were palpable. The patient died, August, 1915. The microscopic and cultural findings were characteristic.

CASE XLII.—Cummins and Sanders (1916). A negro, aged forty-one years, a Pullman chef, who had made several runs over the San Joaquin Valley and always slept in his car, was admitted to the hospital in March, 1915. Two months prior he began to cough and had pain in the region of the left kidney. He lost 20 pounds in one month. Nodules developed in various places. Just before death muscular twitchings and convulsions occurred. Autopsy showed lesions in the occiput, left frontal region, spleen, lung, liver and lymph nodes. The microscopic and cultural findings were characteristic.

CASE XLIII.—Cummins and Sanders (1916). A Mexican laborer, aged twenty-one years, who lived in San Joaquin Valley, was admitted to the hospital in February, 1916. He complained of cough, bloody sputum and a sore right ankle. He left the hospital. The diagnosis was based on smears.

CASE XLIV.—Bowman (1919). A Mexican, aged twenty-five years, worked on a ranch in Bakersfield, Calif. He came to the hospital in February, 1916, with a diagnosis of monarticular rheumatism. He had pain and swelling of the left ankle. The bone was curetted and bloody grandular tissue was removed. The duration was two months. Autopsy showed sinuses leading to the ankle joints and extended upward in the

legs along the tendons. Lesions were found in the lung and intestines. The microscopic and cultural findings were characteristic.

CASE XLV.—Bowman (1919). A negro, aged eighty-three years, who worked about horses in Los Angeles. He entered the hospital in March, 1917, with a painful left ankle. On May 1, his leg was emputated at the middle third. He was discharged June 4. The microscopic and cultural findings were characteristic.

CASE XLVI.—Bowman (1919). A Mexican, aged fifty-four years, who worked on a ranch and cared for horses in Los Angeles. He came to the hospital in May, 1917, with the diagnosis of right psoas abscess and an infected left hand. The duration was one month. The microscopic and cultural findings were characteristic.

CASE XLVII.—Bowman (1919). A male, aged twenty-eight years, Mexican ranch hand in Los Angeles for eight years, had spent three months in San Joaquin Valley. In January, 1917, the left index finger became swollen and very painful. Subcutaneous nodules appeared on the scalp and fingers. Many other joints became involved. The microscopic and cultural findings were characteristic.

CASE XLVIII.—Bowman (1919). A Mexican, aged forty-eight years, worked in cotton in Los Angeles, spent six months in San Joaquin Valley. He came to the hospital in September, 1917, with the diagnosis of ulcer of the foot. He refused amputation. The microscopic and cultural findings were characteristic.

CASE XLIX.—Bowman (1919). A male, aged fifty-four years, who worked with horses and cattle, lived in Visalia, Calif. He came to the hospital in May, 1918, with the diagnosis of "multiple abscesses." In September, 1917, he developed headache, cough, temperature of 105° F. and pustules appeared over the entire body. He lost 65 pounds in nine months. He died in November, 1918. Autopsy revealed lesions in the lung. The microscopic and cultural findings were characteristic.

CASE L.—Helsley (1919). A negro, aged thirty-two years, a waiter for ten years in Sacramento and San Joaquin Valley. In March, 1917, he noticed a large tumor in the left lumbar region and swelling in the right supraclavicle region. The diagnosis was based upon biopsy.

CASE LI.—Lynch (1920). A negress, aged forty-five years, who was born and who had lived on an island near Charleston, S. C. She was admitted to the hospital, December 10, 1918, in a delirious state. She had been treated for influenza. She died, December 12, 1918, with a diagnosis of tuberculosis. Autopsy showed lesions in the lung. The microscopic and cultural findings were characteristic.

CASE LII.—Burkhead (1922). The patient's age, sex, race, occupation and location are not reported. Subcutaneous nodules developed in the neck; the glands also became involved. The patient had a cough and eventually died. The diagnosis was made on the microscopic findings.

CASE LIII.—Hirsch (1923). A negro, aged twenty-seven years, who worked on a Pullman which ran between Chicago and Los Angeles. His symptoms began in March, 1923, with cough, fever and pain in the chest. He developed several abscesses in the mediastinum. He died, May, 1923.

Autopsy showed miliary nodules in the lung, suprarenal and pancreas, and suppurative osteomyelitis. The microscopic and cultural findings were characteristic.

CASE LIV.—Pruett and Wayson (1923). A male, aged fifty-six years, a merchant seaman. He was admitted to the hospital March, 1923, with a diagnosis of tuberculosis. He complained of a swollen knee. He improved with surgical treatment. The microscopic and cultural findings were characteristic.

CASE LV.—Taylor (1923). A negro laborer, aged forty-four years, who had spent eight years in Los Angeles. He came to the hospital in February, 1919, complaining of pain and swelling in the back. There was a bulging mass at the edge of the left quadratus lumborum muscle. The duration was five months. The microscopic and cultural findings were characteristic.

CASE LVI.—Taylor (1923). A Serbian laborer, aged thirty-seven years, who had lived in Los Angeles for nine months. He came to the hospital March, 1919, with multiple skin lesions. He had been in a sanatorium for tuberculosis. His joints became involved. He died May, 1919. Autopsy showed miliary lesions in the kidney, adrenals and lungs. The microscopic and cultural findings were characteristic.

CASE LVII.—Taylor (1923). A male Mexican child, aged three years, who had lived in California. The child was admitted to the hospital in March, 1919, with multiple abscesses and a swollen knee. He died, May, 1923. Autopsy revealed fibrinous pleurisy, miliary granuloma of lungs and meninges. The microscopic and cultural findings were characteristic.

CASE LVIII.—Taylor (1923). A Mexican, aged seventeen years, occupation not given. He was admitted to the hospital, May, 1919, with discharging sinuses under right and left sides of the mandible, right elbow, fifth finger, ankle and toes. The microscopic and cultural findings were characteristic.

CASE LIX.—Taylor (1923). A male, laborer, aged thirty-four years, who had lived in California for two years. He was admitted to the hospital, November, 1919, with swelling of the left knee. His joints were painful and stiff. He developed multiple subcutaneous abscesses and died, February, 1920. The microscopic and cultural findings were characteristic.

CASE LX.—Taylor (1923). A Mexican laborer. The Roentgen ray findings in right ankle are recorded.

CASE LXI.—Taylor (1923). A Russian laborer, aged thirty-seven years, who had lived in California for seven years. He was admitted to the hospital, May, 1920; he had been treated for tuberculosis of the bones of the foot and ankle. In July his leg was amputated. The microscopic and cultural findings were characteristic.

CASE LXII.—Taylor (1923). A Mexican, aged twenty-five years, occupation not given, had lived in California for ten years. He was admitted to the hospital, January, 1921, with fever and difficult breathing. He died February, 1921. Autopsy showed numerous and extensive subcutaneous abscesses, fibropurulent pleuritis and osteomyelitis. The microscopic and cultural findings were characteristic.

CASE LXIII.—Taylor (1923). A Mexican laborer, aged twenty-three years, who had lived in Los Angeles for one year. He was admitted to the hospital February, 1921, with diagnosis of monarticular arthritis. April, 1921, his left leg was amputated. The microscopic and cultural findings were characteristic.

CASE LXIV.—Taylor (1923). A negro cook, aged twenty years, who had lived in California for one year. He was admitted to the hospital in April, 1921, with a diagnosis of pulmonary tuberculosis. He had several abscesses and died in one month. Autopsy showed involvement of both lungs, spleen, liver and kidneys. The microscopic and cultural findings were characteristic.

CASE LXV.—Taylor (1923). A Mexican child, aged nine years, who had lived in California for five years. He was admitted to the hospital April, 1920, with enlarged cervical and inguinal lymph glands. The duration was one month. The microscopic and cultural findings were characteristic.

CASE LXVI.—Hammack and Lacey (1924). A negro gardener, aged eighty-three years, who had lived in California for twenty-five years. The location of the disease was in the left ankle. The leg was amputated, and the microscopic and cultural findings were characteristic.

CASE LXVII.—Hammack and Lacey (1924). A male, Mexican, aged fifty-four years, who had spent one year in San Joaquin Valley, Calif. The location of the disease was in the right groin, vertebræ and left wrist. The duration was one year and the outcome was death.

CASE LXVIII.—Hammack and Lacey (1924). An American, aged twenty-eight years, teamster, who had lived in California all his life. The location of the disease was in the fingers, knee joints and subcutaneous abscesses. The duration was eleven months and the outcome was death. The microscopic and cultural findings were characteristic.

CASE LXIX.—Hammack and Lacey (1924). A Mexican, aged twenty-five years, farm and railroad laborer, who had been in California for six years. The lesions were located in the ankles, lungs, pericardium and subcutaneous abscesses. The duration was four months and the outcome was death. The microscopic and cultural findings were characteristic.

CASE LXX.—Hammack and Lacey (1924). A Mexican, aged forty-eight years, farm laborer, who had lived in California for four years. The lesions were located in the right ankle. The duration was eight months. The outcome was unknown as the patient refused amputation. The microscopic and cultural findings were characteristic.

CASE LXXI.—Hammack and Lacey (1924). A negro laborer, aged forty-four years, who had been in California for eight years. He suffered from abscesses in the lumbar region and in the lumbar vertebræ. The duration was five months and the outcome was death. The microscopic findings were characteristic.

CASE LXXII.—Hammack and Lacey (1924). A Mexican boy, aged eight years, who had been in California all his life. The locations of the lesions were in the ankle, subcutaneous abscesses, lungs and brain. The duration was seven months. The microscopic and cultural findings were characteristic.

CASE LXXIII.—Hammack and Lacey (1924). A Mexican boy, aged three years who had always lived in California. The lesions were located in the toes, elbow, ankle and cervical glands. The duration and outcome were unknown.

CASE LXXIV.—Hammack and Lacey (1924). A male, Serbian, aged thirty-four years, oil worker, who had been in California for three years. The locations of the lesions were in the skin, subcutaneous abscesses, in the wrist, skull and in the kidney. The duration was four months and the outcome was death.

CASE LXXV.—Hammack and Lacey (1924). A Mexican boy, aged nine years, who had been in California for five years. The location of the lesions was in the lymph glands, fingers, ilium, tibia and lung. The duration was four months and the outcome was death. The microscopic and cultural findings were characteristic.

CASE LXXVI.—Hammack and Lacey (1924). An Armenian truck driver, aged twenty-seven years, who had been in California for seven years. Location of lesions in the ankle. The duration was five months before amputation. The microscopic and cultural findings were characteristic.

CASE LXXVII.—Hammack and Lacey (1924). A Mexican, aged thirty-four years, painter, who had been in California for one year. The location of the lesions was in the ankle, knee, sacrum, sternum and subcutaneous abscesses. The duration was four months and the outcome was death. The microscopic and cultural findings were characteristic.

CASE LXXVIII.—Hammack and Lacey (1924). A Mexican, aged twenty-five years, farm laborer, who had been in California for ten years. The location of the lesions was in the vertebræ, ribs, pleura and subcutaneous abscesses. The duration was six months and the outcome fatal. The microscopic and cultural findings were characteristic.

CASE LXXIX.—Hammack and Lacey (1924). A negro, aged twenty-eight years, farm laborer, who had lived in California. The lesions were in the lungs, vertebræ, ribs and subcutaneous abscesses. The duration was one month and the outcome death. The microscopic and cultural findings were characteristic.

CASE LXXX.—Hammack and Lacey (1924). A female, Mexican, aged thirty-four years, who had been in California two years. The disease was located in the ankle. The duration was two years; she refused amputation.

CASE LXXXI.—Hammack and Lacey (1924). An American, aged sixty-one years, electrician, who had been in California for fifteen years. The disease was located in the ankle. The duration was sixteen months before amputation.

CASE LXXXII.—Hammack and Lacey (1924). A Mexican girl, aged two years, who had been four months in California. The location of the disease was in the humerus. The limb was amputated.

CASE LXXXIII.—Hammack and Lacey (1924). An American, aged thirty-nine years, clerk, who had never been in California but who had

been in Arizona. The location of the disease was in the form of subcutaneous abscesses in the muscles of the neck.

CASE LXXXIV.—Hammack and Lacey (1924). An American woman, aged sixty-one years, who had been in California for thirty years. The location of the disease was in the head of the radius and vulva. The duration was one year.

CASE LXXXV.—Hammack and Lacey (1924). A male, American, aged fifty-three years, who was a veterinarian and farm laborer, had been in California for fourteen years. The disease was in the form of subcutaneous abscesses in the wrist. The duration was four years. After being treated by drainage, the lesions healed and the patient is living.

CASE LXXXVI.—Hammack and Lacey (1924). A female, American, aged twenty-three years, had lived in California all her life. Lesions were found in the lung, cervical glands and subcutaneous abscesses. The duration was twenty months. The patient has remained well for five years.

CASE LXXXVII.—Hammack and Lacey (1924). A male, American, aged twenty-three years, without occupation, had been in California for two months. Lesions were found in the ankle. The duration was one month before amputation. Abscesses followed four months later. The patient has remained well for nine years.

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THE EMPTYING OF THE GALL BLADDER: AN EXPERIMENTAL STUDY.*

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The actual experimental proof of the function of the gall bladder has been elusive and the difficulty of obtaining it has furnished an increasing source of inspiration to those interested in the physiology and pathology of the biliary system. Some of the suggestions regarding the function of the gall bladder are that it regulates the flow of bile, that it regulates pressure, that it is a reservoir, that it secretes a specific secretion, and that it concentrates bile.[23]

The experiments reviewed herewith were made in a study of the normal emptying of the gall bladder as seen by the Roentgen ray during digestion. Many investigators have reasoned that the gall bladder empties its bile through the common bile duct into the duodenum. Others, because of lack of undoubted experimental proof to the contrary, believe that the bile does not leave the gall bladder by the channels through which it enters.

Review of Previous Work. Some of the earlier experimental work on the gall bladder was done to ascertain whether it could be made to contract. Conflicting views have been recorded by various writers with regard to the innervation of the gall bladder. Among these investigators are Doyon, Westphal, Freese, and Bainbridge and Dale. Meltzer asserted that the sphincter of Oddi relaxes at the time the gall bladder contracts, that is, according to the law of contrary innervation. The experimental evidence thus far recorded seems to show that the vagus nerve is mainly motor to the gall bladder and the splanchnic nerve mainly inhibitory.

Doyon was the first to record graphically the rhythmic variations in pressure of the gall bladder. Bainbridge and Dale noted the rhythmic variations at the rate of 1 to 3. Potter and Mann, Okaka, Taylor and Wilson, and others, have noted similar rhythmic changes.

A study of the gall bladder from standpoints other than its nervous mechanism has been productive. Potter and Mann have shown experimentally on dogs a reciprocal pressure relation between the gall bladder and common duct. After injection of barium into the gall bladder through a cholecystostomy tube and examination of the area by means of the fluoroscope, it was noted that spurts of

* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery, 1926.

Work done in the Division of Experimental Surgery and Pathology.
Submitted for publication February 17, 1927.

opaque material were projected at intervals through the neck of the gall bladder. More recently McMaster and Elman have corroborated and enlarged on these observations. Within from two to ten minutes after feeding, and even earlier, they noted a rapid increase in pressure of the gall bladder and a fall in a varying short time to a former level. It was observed that this phenomenon was repeated at varying intervals. It was also shown that simultaneous with increase in pressure of the gall bladder the resistance of the sphincter, at the distal end of the common duct, is lowered. These authors believe that the contractions of the musculature of the gall bladder are the main factors causing expulsion of bile. Okada also observed that during digestion there is an increase in the force and rhythm of the contractions of the gall bladder. Rous and McMaster demonstrated conclusively the remarkable absorptive powers of the gall bladder which act to concentrate its bile to about eight times that in the hepatic duct. Lyon, investigating along different lines, has accumulated much data to show that nonsurgical biliary drainage takes place following the instillation, by a duodenal tube, of a concentrated solution of magnesium sulphate into the duodenum at the ampulla of Vater. He believes that the gall bladder can be emptied through the cystic and common ducts in this manner. Silverman and Menville supported this idea. They used the Graham-Cole technique of cholecystography.

Oddly enough, the most outstanding dispute among those who have studied the function of the gall bladder is with reference to the manner in which the gall bladder empties. Sweet, in this country, and Halpert and others in Europe, independently, in 1924, concluded that the gall bladder does not empty through the channels by which the bile enters it. Sweet believes that the kink in the cystic duct and the valves of Heister are designed to delay the emptying of the gall bladder by external pressure. He concludes that the structure of the gall bladder is responsible for its function of absorption. The position of the fundus suggests inflow rather than outflow. Halpert reasons that normally the bile is absorbed in the intestine but during the interval between periods of digestion it is a function of the gall bladder to absorb it, probably through the mucosa to the lymph and then to the blood. Berg believes that bile is concentrated in order to regulate pressure in the bile passages. Halpert quotes Stansky as believing that bile is absorbed in the gall bladder.

By far the greater number of investigators believe that the contents of the gall bladder are emptied through the cystic and common ducts into the duodenum. There is, however, much controversy as to the method of emptying. Harer, Hargis and van Meter concluded that if the gall bladder empties through the cystic duct it is a result of distention and congestion of the adjacent organs during digestion and of the milking action of peristaltic

waves. Diamond regards the gall bladder as a receptable for overflow, in the nature of a diverticulum of the common duct devoid of contractile power. Auster and Crohn, by injecting suspensions of carmine powder and charcoal into the gall bladder, presented evidence of its emptying through the duct, and assert that the musculature of the gall bladder is scanty and has poor contractile power. Winkelstein, and Winkelstein and Aschner, have been the chief advocates in America of the idea that internal pressure changes such as result from respiration are mainly responsible for the emptying of the gall bladder, and that the contractions are of little or no significance. Abramson, by injecting solutions of silver iodide and neosilvol into the gall bladder of dogs by means of a cholecystostomy tube, found that the ordinary movements of the dog produced no expulsion of material from the gall bladder. In one of the experiments he observed, by means of the fluoroscope, that material inside the gall bladder distended the cystic and common ducts and passed into the duodenum, being slowly propelled by the peristalsis of the duct. This observation was not repeated. More recently, in articles by Graham; Copher and Kodama; Graham, Cole, Copher and Kodama; and Copher, Kodama and Graham, little or no importance is attached to contractions of the gall bladder. Their idea is that the emptying of the gall bladder is chiefly a passive phenomenon due to factors such as the elastic recoil of a distensible viscus and the gradual washing out of its contents by the ingress of fresh bile from the liver. The spurting of the bile through the ampulla of Vater is believed to be due largely to the milking action of the duodenal peristaltic waves on the common duct, which passes obliquely through the duodenal wall. Changes in intraäbdominal pressure are also considered significant.

Among those who have recently presented evidence to show that the gall bladder empties normally, largely by its own contractions, are Higgins and Mann; Whitaker and Boyden;[6, 34, 35] Sosman, Whitaker and Edson; and McMaster and Elman. Chiray and Pavel deduce from their clinical observations that the gall bladder is one of the slowest of contracting mechanisms, and that contraction or spasm of its musculature is a factor in gall bladder colic. Boyden noted that the gall bladders of cats, killed at certain intervals following the ingestion of a mixture of milk and cream, were practically empty. He found that the gall bladder emptied its contents gradually over a period of one and three-fourths hours following the feeding of a mixture of egg yolk and cream, and that after approximately five hours the vesicle refilled slowly. These observations, which proved that the gall bladder does empty, also suggested a method for studying the mechanism of the emptying. Sosman, Whitaker and Edson observed the effect of different factors on the change in the shadow of the gall bladder in roentgeno-

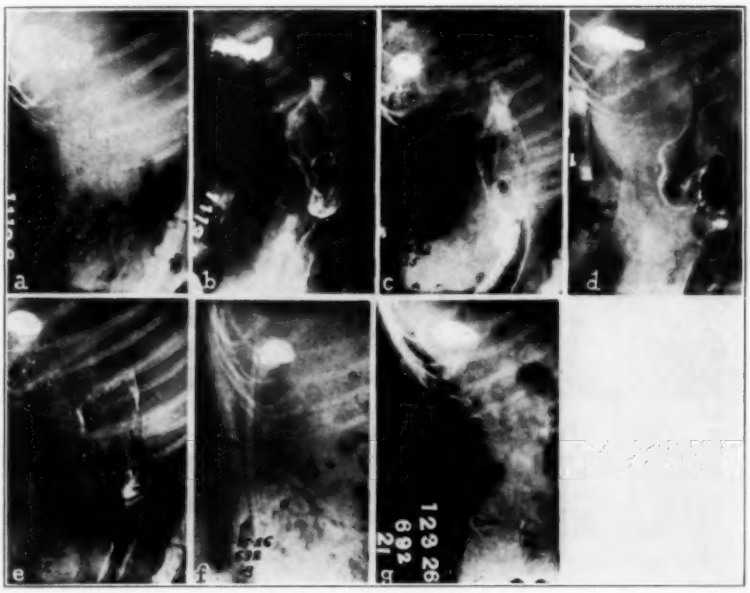

FIG. 1.—Emptying of the gall bladder. *a*, Gall bladder before emptying, as a result of feeding. *b*, *c*, *d*, and *e*, taken at two and a half hours, four hours, six hours and eight hours, respectively, after feeding egg yolk and cream mixture show much 40 per cent iodized oil in the small bowel. *f* and *g*, taken with the animal in a fasting state on the second and eighth day, respectively, after feeding.

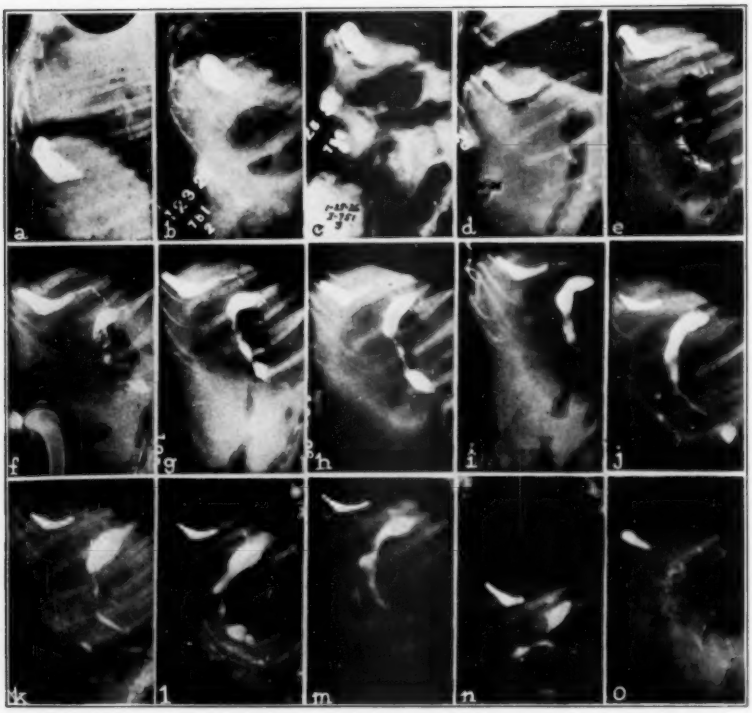

FIG. 2.—Active emptying of the gall bladder after feeding. *a* and *b*, films taken with the dog fasting on the second and third days after operation. *c* shows film with vesical shadow on the fourth day after operation just before feeding egg yolk and cream mixture. Films from *d* to *o* were taken consecutively from fifteen to twenty-five minutes after feeding. Film *o* was taken three hours after feeding. Characteristic elongation of the shadow of the gall bladder with active emptying is shown. The cystic and common ducts are well outlined by 40 per cent iodized oil passing down their paths. Oil is also seen in the small bowel.

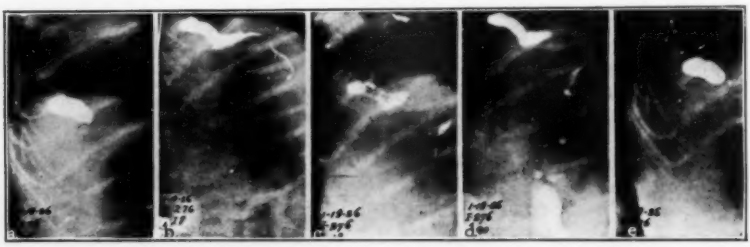

FIG. 3.—Emptying of the gall bladder. Film *a* was taken fifteen minutes after a second feeding of egg yolk and cream mixture. Films *b*, *c*, *d*, and *e* were taken thirty, thirty-eight, and forty-five minutes, and one hour consecutively after feeding. This series shows the gall bladder emptying a small portion of its contents, then remaining in a contracted state for a considerable period and regaining its noncontractile appearance within an hour.

grams. Observations were made on human beings and on dogs. Sight, smell and taste of food, a carbohydrate meal, abdominal pressure changes, and external and internal heat and cold, had no effect on the shadow of the gall bladder in the roentgenogram. The irritation of a duodenal tube in an excitable subject was followed by a moderate decrease in the size of the shadow; this possibly was due to retching. There was a marked decrease and disappearance of the shadow following the injection of food rich in fat. In later studies by Boyden and Whitaker, it was shown that successive cholecystograms from a given subject suggested that the gall bladder did not empty continuously, but periodically. In cats that had been fasting for twenty-four hours previous to laparotomy the gall bladder was opened, emptied of bile, refilled with iodized oil, and the opening sewed up. About twenty-four hours later, feeding tests were made. Roentgenograms taken at frequent intervals after feeding the egg yolk showed the gall bladder emptying into the duodenum through the duct. This usually occurred within from five to thirty minutes after feeding and at varying intervals for varying lengths of time. They concluded that contractions of the gall bladder are responsible for its normal emptying.

Experimental Methods. Dogs were used in all of my experiments. Because 40 per cent iodized oil is nonirritant and causes dense shadows in roentgenograms, it was selected for injection into the gall bladder. Boyden's methods of feeding were used to produce the emptying of the gall bladder during digestion.

The animals were fasted for twenty-four hours previous to operation. The abdomen was opened under ether anesthesia and strict aseptic technique, and the gall bladder, with the surrounding lobes of liver, was delivered into the wound. Forty per cent iodized oil was injected into the gall bladder after an equal amount of bile had been withdrawn. In all but one case the needle was inserted into the gall bladder first through one edge of the liver and then into the gall bladder only where it is attached to the liver by Glisson's capsule. This did not disturb the musculature of the gall bladder and controlled the leakage of bile. The slight oozing, if any, from the liver was soon stopped by the gloved finger held over the area. This technique does not necessitate suturing or clamping of the wall of the gall bladder and apparently is ideal for intravesical injection in functional studies of the gall bladder. The animals were fasted after operation until observations were to be made. All factors were kept as constant as possible.

Results. Each day during the fasting period roentgenograms of the gall bladder were made. With one exception there was no evidence of emptying of the gall bladder. A feeding of 300 to 500 cc. of egg yolk and cream mixture, depending on the size of the animal, was given for the first observation following fasting. In other dogs mechanical factors influencing expulsion of bile from the

gall bladder were usually observed on the day previous to the feeding. Following the feeding, roentgenograms were made at from ten to twenty-minute intervals and fluoroscopic observations at more frequent intervals. Emptying of the gall bladder could be seen in all the dogs following the ingestion of the egg yolk and cream mixture (Fig. 1). In some instances a second feeding was given before emptying took place. Usually within from ten to forty-five minutes the gall bladder emptied through the cystic and common ducts into the duodenum, as shown fluoroscopically and roentgenographically. Just before or during emptying the shadow of the vesicle was elongated, pointing toward the cystic duct. Such contortion is characteristic and no doubt indicates intrinsic contraction of the musculature. The duct was well outlined in a number of roentgenograms as a result of the active emptying of the gall bladder into the cystic and common ducts following feeding. Emptying did not continue uniformly with digestion, the material being expelled from the vesicle at varying intervals following the ingestion of food.

There was no definite evidence that ordinary movements of the animals caused expulsion of material from the gall bladder. Repeated firm external pressure over the area of the gall bladder with the hands, in several instances did not appear to expel the content of the vesicle except in one instance in which the action of the sphincter was eliminated. Also pressure over the area of the gall bladder, when the stomach was well filled with water, did not appear to expel the material. There was no evidence that respiratory movements caused emptying of the gall bladder in any of the animals. Roentgenograms taken following vomiting in several instances did not show emptying when the influence of the passage of a stomach tube was not a factor; neither was it caused by the act of defecation. Evidence of emptying of the gall bladder was determined on the basis of actually seeing the opaque material either in the bile duct or in the intestinal tract. It may thus be asserted that ordinary changes of internal and external pressure do not cause expulsion of material from the gall bladder, as seen by fluoroscopic and roentgenologic examination.

Passage of a stomach tube resulted in definite expulsion of material from the gall bladder in a number of animals. Other irritating maneuvers, as filling the stomach with air, aspiration of the content, and manipulation of the stomach tube, caused the expulsion of a slight amount of material. Filling the stomach with water by means of a stomach tube caused expulsion in several instances. These observations are similar to those recorded by Boyden who recognized in cats the partial emptying of the vesicle on such external stimulations as the insertion of a needle or shaving of the part preliminary to injection. If the dog voluntarily drank a large quantity of water no material passed from the gall bladder. Marked

pressure over the area of the gall bladder after the dog had become accustomed to the stomach tube, which had remained in place for some time, did not expel any of the content.

In one experiment a rubber tube was fixed in place at operation so that it extended from the lower portion of the common duct through the sphincter into the lumen of the duodenum. The tube kept the sphincter at the lower end of the common duct continuously open. The shadow of the gall bladder, as shown in the roentgenograms, was smaller during the two days after operation on which the animal fasted. Marked external pressure over the region of the gall bladder caused the expulsion of some material in one instance, but it could not be repeated in the same animal. The gall bladder emptied in the usual way following feeding. The roentgenograms taken after feeding showed the emptying to be more active in some cases than in others, which suggest intrinsic periodic or rhythmic contraction of the musculature of the gall bladder.

Discussion. The appearance of shadows in roentgenograms taken in the area of the gall bladder during the foregoing experiments leaves little doubt that the wall of the gall bladder does undergo contraction during digestion, thereby tending to empty its contents. Just preceding the emptying, the neck of the gall bladder appears to elongate toward the cystic duct. Also the complete shadow of the gall bladder is longer and narrower (Figs. 2 and 3). Roentgenographic and fluoroscopic observations over a considerable period indicate that the gall bladder may remain for some time in a contracted or increased tonic state, as shown by the shape and more or less elongated neck. Although the neck of the gall bladder may be characteristically drawn out to a cone-shaped point, there is no evidence of a continuous steady emptying. On the contrary, intervals in which material is seen passing down the ducts are interspersed with intervals of varying length in which no material is seen to pass through the cystic and common ducts. This later interval may vary from a few minutes to much longer. In one instance the first passage of 40 per cent iodized oil from the gall bladder was noted during the first hour after feeding. Following this there was an interval of almost an hour during which there was no evidence of material having passed down the ducts. In the roentgenogram the gall bladder appeared to be in a semiresting state, a little elongated but with the neck rounded or stubbed off instead of stringlike, as when it was emptying into the cystic and common ducts. After the longer interval the neck became drawn out again and emptied for a short period. It might be assumed that the sphincter at the lower end of the common duct is a possible factor in producing this interesting finding. Other factors may account for the longer interval mentioned. In several of the roentgenograms the neck of the gall bladder could be seen elongated to a stringlike shadow with dense areas of material in the ampulla

and duodenum. In close association with, or adjoining, the shadow of the duodenum or ampulla, in the same roentgenogram small globules of 40 per cent iodized oil adjacent to each other could be seen. They stood out clear and sharp against the rather blurred irregular longer shadow denoting the area of the duodenum and ampulla. It is possible that these globules of 40 per cent iodized oil were in the lower end of the common duct just above the sphincter, being prevented from entering the duodenum by an increase in tone of the sphincter before they had finished their journey to the lumen of the small bowel.

Positive proof that respiration is a factor in the normal emptying of the gall bladder was not brought out in these experiments. Under the fluoroscope the globules of opaque material passing down the ducts during digestion did not have an ebb and flow rhythm, as one would expect if the emptying were taking place as a result of respiration. On the contrary, the material appeared little, if at all, affected by respiratory movements.

That bile tends to remain in the gall bladder during the fasting state is shown in the roentgenograms taken each day for from two to four days following operation while the dog was fasting. With one or two exceptions there was no evidence of 40 per cent iodized oil in the bowels or of its having left the gall bladder during these rather long periods of fasting. The exceptions suggest a possible overflow of the gall bladder, extravesical irritation, or some unknown factor.

On different occasions in the course of the experiments marked external abdominal pressure was applied over the region of the gall bladder by pushing downward with the hands, and fluoroscopic and roentgenographic observations made immediately afterward. No evidence that this caused expulsion of material from the gall bladder was obtained. On one occasion in which a large stomach tube alone was used, it was noted that some iodized oil passed from the gall bladder as a result of the manipulation. In several other cases, following instillations of water into the stomach through a stomach tube or by the insertion of the stomach tube alone 40 per cent iodized oil globules from the gall bladder could be seen in the duodenum or ducts. It is possible that the reflex irritation set up by the tube in the stomach may have caused some emptying independent of increased intraäbdominal pressure due to retching. Another possible, but not probable, explanation would be that the irritation of the tube caused inhibition of sphincter tone, allowing intraäbdominal pressure resulting from retching to cause expulsion of some material from the gall bladder into the duodenum. With the stomach tube in place there may be a change in the pressure relations of the abdominal cavity. It might also have been due to a vasomotor reflex involving the liver and thus secondarily pressing on the gall bladder. Nothing to indicate emptying of the gall

bladder was found in roentgenograms taken immediately after vomiting had occurred when no stomach tube had been passed. External pressure over the area of the gall bladder with stomach tube in place after the dog had become accustomed to the tube gave no evidence of causing expulsion of material from the gall bladder.

It should be mentioned that in the comparison of fluoroscopic and roentgenographic observations other interesting features were suggested. In one dog the gall bladder was emptying through the cystic and common ducts. The gall bladder was elongated with the neck drawn out in a cone shape. Little globules of 40 per cent iodized oil were seen to cut away from the upper thread-like shadow and glide rapidly down the duct in a sausage string formation to the lower dense shadow which marked out the area of the duodenum and ampulla. This would last for varying periods. On two occasions I left the room and came back after about two minutes, and although the dog lay quietly on the table during the intervening time the coursing of the 40 per cent iodized oil down the duct had stopped. On each occasion additional persons came into the observation room. This suggested the possibility that psychic manifestations in the canine mechanism may have played a part in the stoppage of biliary flow. Also in the same animal immediately after the oil had been shown to be passing down the duct a roentgenogram was made which showed the neck of the gall bladder elongated to a stringlike shadow but without droplets of the oil in the common duct. Dense shadows of the oil were plainly shown in the area of the duodenum and ampulla. Moving the dog about in order to place Roentgen ray plates and the bustle of switching the machines may have been a factor in stopping the flow. This was noted several times in two of the dogs who were very apprehensive, and thus again it is suggested that psychic factors may also play some part in biliary flow.

In an interesting experiment 40 per cent iodized oil was injected into the gall bladder in the usual way and at the same operation the duodenum was opened opposite the sphincter of Oddi and a rubber tube fixed in place so that it extended from the lower end of the common duct through the sphincter region into the lumen of the duodenum. This prevented the action of the sphincter at the lower end of the common duct. The abdomen was closed and the dog was kept in the fasting state for two days while he recovered from the immediate effects of the operation. During this interval there was evidence that the gall bladder had expelled some of its contents, as shown by the reduction in the size of its shadow. This was in contradistinction to most of the results obtained in the fasting animal with the sphincter of Oddi intact. On one occasion in this same animal marked pressure over the area of the gall bladder caused expulsion of some of its contents, but this could not be repeated. Other mechanical factors, such as passing the stomach tube, manipu-

lation of the tube and filling the stomach with air, caused expulsion of some of the contents of the gall bladder. The next day, under the stimulus of feeding, there was evidence in the roentgenograms that the gall bladder emptied slowly over a two-hour period. Some of the roentgenograms showed more active emptying than others, with the duct completely outlined, indicating that at this time the vesicle was undergoing active contraction. Other roentgenograms in the same series showed only a globule or so of the oil in the ducts and the neck of the gall bladder elongated but coming more to a blunt point in contradistinction to the more drawn-out stringlike shadow including the neck and cystic duct in the apparently more

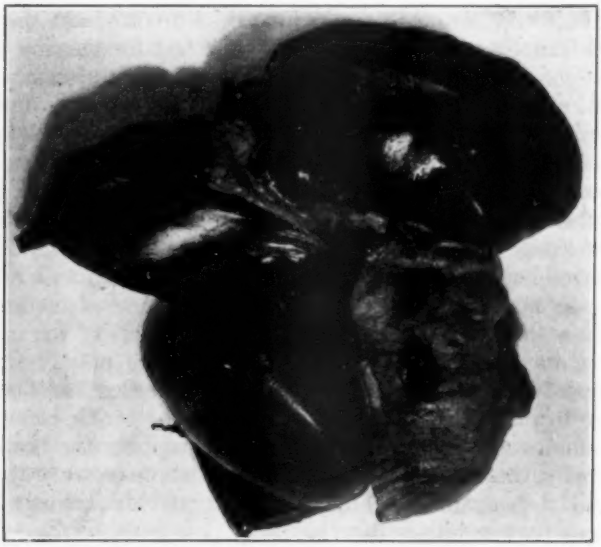

FIG. 4.—Necropsy specimen from an animal in which the sphincter at the lower end of the common duct was eliminated by fixing a tube at operation so that it extended from the lower portion of the common duct through the sphincter into the lumen of the bowel. The animal was killed on the fourth day after operation and five hours after feeding. The gall bladder was markedly contracted and practically empty as a result of feeding. The end of the tube is shown extending through the sphincter just as it was fixed at operation.

active contracting gall bladders. This suggests an important intrinsic periodic contraction of the musculature of the gall bladder which is brought into play with digestion. In this animal, when the action of the sphincter was thrown out by means of the rubber tube, definite emptying took place as a result of these so-called periodic contractions. It is likely that the sphincter at the lower end of the common duct is relaxed when the periodic or rhythmic contraction of the gall bladder causes it to empty. No definite evidence that the gall bladder emptied as a result of respiratory movements could be determined in this experiment with the sphincter at the lower end of the common duct continuously open.

PROTOCOL.—DOG I 983, WEIGHT 5.2 KG. OPERATION MARCH 22, 1926. ASPIRATION OF 8 CC. OF BILE FROM GALL BLADDER AND INJECTION OF 5 CC. OF 40 PER CENT IODIZED OIL INTO GALL BLADDER.

Roentgen ray.	Time.	Date.	Remarks.
	A.M.		
1	....	3–22–26	Just after operation. No emptying.
2	....	3–23–26	No emptying.
3	....	3–24–26	No emptying.
4	8:59	3–25–26	Dog fasted without water twenty-four hours. Gall bladder short sausage shape. No emptying.
5	9:00	....	Just after marked abdominal pressure. Shadow of gall bladder area about the same. No emptying.
6	9:10	....	Ten minutes later. Picture about same as above.
7	9:13	....	Just after marked abdominal pressure. No emptying.
8	9:45	....	Thirty minutes later. No emptying.
9	9:50	....	Just after drinking 200 cc. of water voluntarily. No emptying. Neck of gall bladder blunt handle-like appearance.
10	9:55	....	After marked abdominal pressure. No emptying.
11	10:05	....	Ten minutes later. No emptying.
12	10:10	....	After marked abdominal pressure. No emptying.
13	10:25	....	Fifteen minutes later. No emptying. Neck of gall bladder slightly elongated but rounded off.
14	10:35	....	After passing stomach tube. Much water came back. Elongated shadow of iodized oil seen in duct. Expulsion of material as result of passage of stomach tube. Shadow of gall bladder area cone shaped and little more elongated than last.
15	10:52	....	Stomach tube still in place. No evidence of emptying since last picture. Shadow of gall bladder area a little longer.
16	11:10	....	Stomach tube still in place. No evidence of emptying.
17	11:15	....	Stomach tube still in place. Marked abdominal pressure just before roentgenogram. No evidence of gall bladder emptying.
18	11:30	....	Fifteen minutes later. Tube still in place. No emptying.
19	11:32	....	After marked abdominal pressure. Stomach tube still in place. No evidence of emptying. Shadow of neck of gall bladder more rounded off.
20	11:42	....	Ten minutes later. No evidence of emptying.
21	11:45	....	After aspiration of end of tube with syringe. Small droplet of oil seen in lower portion of duct.
22	11:50	....	Five minutes later. No evidence of emptying. Poor picture. Dog moved.
23	11:55	....	After filling stomach with air. Much retching. No evidence of emptying.
24	12:00	....	Five minutes later. Long strand of oil seen in duct.
	P.M.		
25	12:03	....	After much manipulation of tube in stomach. Strand of oil in duct as in last picture. No material seen in small bowel.
26	1:48	....	Just before taking 300 cc. of egg yolk and cream (1:50 P.M.) voluntarily.
27	1:55	....	Just after feeding. No evidence of emptying.
28	2:10	....	Fifteen minutes after feeding. Neck of gall bladder somewhat elongated but with rounded blunt end. Scattered shadows of oil in small bowel.
29	2:30	....	Forty minutes after feeding. No definite shadows of oil in small bowel. Neck of gall bladder not quite so elongated as in last picture.
30	2:45	....	Oil seen in small bowel by fluoroscope just before this picture. Also peristaltic movements in small bowel. Shadow of gall bladder area somewhat narrowed and elongated; small point at cystic duct entrance.

PROTOCOL.—DOG I 983, WEIGHT 5.2 KG. OPERATION MARCH 22, 1926. ASPIRATION OF 8 CC. OF BILE FROM GALL BLADDER AND INJECTION OF 5 CC. OF 40 PER CENT IODIZED OIL INTO GALL BLADDER—(*Continued*).

Roentgen ray.	Time.	Date.	Remarks.
31	3:00	....	Just before taking of 100 cc. of egg yolk and cream (3:05 P.M.) voluntarily. Few faint scattered shadows of oil in area of small bowel.
32	3:10	....	Just after feeding. Small faint shadow of oil in a area of small bowel.
33	3:33	....	Oil seen by fluoroscope going down duct just previous to roentgenogram. Numerous scattered areas of oil in small bowel. Oil seen in common duct. Shadow of gall bladder area elongated, narrowed and slightly curved. Neck bluntly rounded off.
34	3:37	....	Oil seen by fluoroscope going down duct just before roentgenogram. Shadow of gall bladder area much like last picture. Small droplet of oil seen in common duct. Numerous scattered shadows of oil in small bowel.
35	3:55	....	Just before taking of 40 cc. of egg yolk and cream (4:00 P.M.) voluntarily.
36	4:15	....	Shadow of gall bladder area elongated and somewhat narrowed and curved. Shadow of neck of gall bladder drawn out to a linear shadow pointing craniodorsally. Numerous scattered shadows of oil in area of small bowel.
37	4:40	....	Area of gall bladder still somewhat narrowed but neck bluntly rounded. Few faint shadows of oil in small bowel.
38	A.M. 10:55	3-26-26	Next day. Dog fasted since previous day. Shadow of gall bladder area short with ends rounded. Faint shadow of oil in area of small bowel.
39	P.M. 4:00	3-29-26	Dog fasted since last picture. Shadow of gall bladder short with ends bluntly rounded. No shadows of oil in small bowel.
40	4:15	....	Dog kept in upright posture since last picture.
41	4:20	....	Just after passage of stomach tube. Shadow of gall bladder short and rounded. Oil seen in lower portion of common duct. Another shadow of oil apparently in area of ampulla of duodenum. Stomach tube in place.
42	4:32	....	After dog was kept in upright position for fifteen minutes with stomach tube in place. Faint scattered shadows of oil in small bowel. No evidence of emptying from gall bladder since last picture.
43	4:40	....	After aspiration of contents with tube remaining in place. Much retching. Shadow of gall bladder area short and rounded. Difficult to say whether there was any emptying. Faint small globule-like shadow in lower portion of common duct area but may be in small bowel.
44	4:50	....	Just after passing tube again. Tube came out. Dense small globule-like shadow of oil in common duct, probably just expelled from gall bladder. Shadow of gall bladder area little longer than last with rounded ends.
45	4:55	....	After distending stomach with air. Stomach tube in place. Same narrow elongated shadow of oil in common duct area, in much the same place as before. No well-marked shadows of oil made out in small bowel.
46	5:00	....	After removing tube. Two small globules of oil seen together in common duct. No clear-cut shadows made out in small bowel.

The animal was killed under ether after the feeding. Necropsy showed the gall bladder to be markedly contracted and almost empty. The rubber tube was seen extending from the lower end of the common duct into the lumen of the duodenum through the sphincter, as it had been fixed at operation (Fig. 4).

At best 40 per cent iodized oil is only iodin in an oily vehicle with specific gravity a little greater than gall bladder bile. The emulsion apparently keeps its identity as such while mixed with the contents of the vesicle, but it is nonirritant and tends to follow the normal conduct of the contents of the biliary bladder. It was found to be a more acceptable medium than concentrated solutions of sodium iodid or the tetraphenolphthalein dyes in this experimental cholecystography to study the gall bladder from a functional standpoint.

Summary. The gall bladder empties a portion of its contents into the duodenum with digestion. The contents pass to the duodenum through the cystic and common ducts. It is evident that the emptying of the gall bladder with digestion is intermittent. Periods of active emptying were usually short and could be definitely limited over a varying period. Emptying began within ten to forty-five minutes after feeding and was interspaced with varying intervals in which there was none. From these studies contractions of the musculature of the gall bladder appear to be the main factor in the normal emptying, and intrinsic periodic contractions appear to be important features brought into play with digestion. There is ample evidence that the gall bladder does not tend to expel its contents during the fasting state. Respiratory movements as well as changes in external and intraäbdominal pressure have only a minor part, if any, in the normal emptying. Mechanical factors, such as passing a stomach tube, filling the stomach with air, aspiration of the stomach, and manipulation of the stomach tube in the stomach, caused the definite passage of some material from the gall bladder in several instances, in contrast to the inability to cause expulsion of material from the gall bladder from ordinary changes in intraäbdominal and extraäbdominal pressure.

The sphincter at the lower end of the common duct is possibly one of the factors concerned in the regulation of the flow of bile from the gall bladder although its action is not necessary for the emptying of the gall bladder with digestion. External abdominal pressure caused some expulsion of the contents of the gall bladder in one instance when the sphincter at the lower end of the common duct was eliminated, but feeding was necessary to cause marked emptying of the vesicle.

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BACTEREMIA DUE TO BACILLUS FECALIS ALKALIGENES.

With Report of a Case.

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Systemic infection with Bacillus fecalis alkaligenes is a rare disease; only 40 undoubted cases have been reported in the literature, and of this number only 1 has been reported in the United States.

As typhoid vaccination is being used more extensively, Shearman[20] and Hirst[7] are of the opinion that more and more obscure fevers will be found due to this organism, Bacillus coli and allied groups. It is probable that some of the obscure fevers in our southern states may be due to Bacillus fecalis.

On account of the rarity of the disease a brief résumé of the undoubted cases and also the probable cases is given and we have added 1 undoubted case of our own.

In 1889 Petruschky[14] recovered an organism from stale beer, but it was not until 1896 that he again isolated it and at this time gave it the name of Bacillus fecalis alkaligenes. This organism was found in the feces of ill subjects or those suspected of typhoid fever and occurred either alone or in association with Bacillus typhosus.

Both Pollak[15] and Altschüler[1] in their early works confused this organism with Bacillus typhosus.

In 1902 Petruschky[14] isolated it from six rose spots in a patient with typhoid, while in 1904 Altschüler[1] obtained it in pure culture from the urine of a typhoid patient. Up to this time the Bacillus

fecalis alkaligenes was apparently looked upon as a harmless saprophyte.

In 1908 Lafforgue[9] published an observation of a patient with clinical manifestations of typhoid, rose spots, hypertrophy of the spleen, intestinal hemorrhages and a characteristic temperature curve. A bacillus was obtained in the blood culture which was agglutinated by the patient's serum in 1 to 150 dilution, but neither the typhoid bacillus nor the paratyphoid bacilli were agglutinated. While this organism caused decided alkalization on certain media and presented the characteristics of Bacillus fecalis alkaligenes, yet it appeared to differ in its absence of virulence toward laboratory animals and its action on certain sugars. In view of these facts, some authors have expressed a doubt as to the identity of the bacillus of Lafforgue with Bacillus fecalis alkaligenes.

Fürth,[5] a doctor in the German navy, published, in 1913, 6 cases of general infection with Bacillus fecalis alkaligenes. These infections were observed in sailors in oriental Asia during August, 1912. A bacterium identical with Bacillus fecalis alkaligenes was isolated from a patient on the sixth day and from the feces of another on the twenty-first day of the illness. The serum of the patients agglutinated this organism between 1 and 30 and 1 to 80, but did not agglutinate the typhoid or paratyphoid A and B bacilli or numerous colon bacilli isolated from the stools. The serum of the third patient agglutinated this bacillus in 1 to 60 on the sixth day and 1 to 120 on the eighteenth day, but showed no agglutination of the typhoid or paratyphoid A and B bacilli. The other 3 patients belonged to the same division of the cruiser, showed similar clinical signs, were submitted to same living conditions, and were constantly in close relations. The illness of the latter group appeared fifteen days after the first.

In 1914 Staub and Krais[21] published reports of 2 cases (1 man and 1 woman) of Bacillus fecalis alkaligenes bacteremia. The organism was obtained from the blood of 1 and from the urine of the other and the serum of the respective patients agglutinated this bacillus. These sera did not agglutinate typhoid or paratyphoid bacilli.

Rochaix and Marrotte,[18] in 1915, obtained Bacillus fecalis alkaligenes from the blood of 2 patients. The blood sera agglutinated the organisms in high dilutions, 1 to 1200 and 1 to 1500 respectively, and, while they agglutinated the Bacillus typhosus, the degree of agglutination was feeble. There was no agglutination of paratyphoid bacilli A and B. Crossed agglutination tests were made, the serum of one agglutinating the organisms of the other and reciprocally.

Shearman and Moorehead,[20] in 1916, published reports of 11 cases where Bacillus fecalis was obtained in blood cultures. These

patients were observed in a military hospital in Egypt and all had typhoidal symptoms. The organism was agglutinated by the serum of the patients in high dilutions.

Later, in the same year, Hirst,[7] while working on typhoid carriers at the Military Laboratory, Alexandria, "was surprised at the frequency with which this organism is found in the stools of convalescent cases of enteric in Egypt." In subsequent work he succeeded in isolating the organism in pure culture from the blood of twelve patients. During 1916, in a series of 622 blood cultures, Bacillis fecalis was isolated 23 times out of a total of 123 positive cultures, *i. e.*, 18.7 per cent Bacillus coli was found 12 times and the remaining 88 were organisms of the typhoid group, Bacillus typhosus and paratyphoid A and B.

Hirst[7] also reported 3 additional cases of systemic infection with Bacillus fecalis alkaligenes, which were observed by Wiltshire in another General Hospital in Alexandria.

During June, 1919, Webster[22] observed 11 nursing infants ill with severe diarrhea or having blood in the stools. With blood cultures obtained by puncture of the sagittal sinus by traversing the fontanelle, or by puncture of the external jugular veins, the Bacillus fecalis was obtained 3 times. The ages of the babies were two and a half months, ten months and eleven months. The latter baby died. In the absence of agglutination tests it would be difficult to affirm that Bacillus fecalis was the causal organism in these cases, although it is probable.

De Magalhaes,[2] in 1921, recovered Bacillus fecalis in blood cultures from a patient ill with clinical symptoms of typhoid. This organism was agglutinated by the patient's serum in dilutions up to 1 to 400, but showed no agglutination with typhoid or paratyphoid sera.

In 1921 Watson[23] reported 4 interesting cases observed in soldiers in India. In all of the cases Bacillus fecalis was obtained in the blood cultures. The first case was clinically typhoid. There was continued fever for eighteen days, reaching 104° F. during the first week, then becoming remittent in type and falling by lysis, followed by a typical relapse lasting three weeks, in which the temperature ran somewhat lower than the first course. Abdominal distention and rose spots were present. His serum agglutinated Bacillus paratyphosus A in dilution of 1 to 2000. Eight months later the agglutination with para A was 1 to 100, and with the Bacillus fecalis 1 to 20.

The second case suffered from initial fever of fourteen days, falling by lysis and immediately followed by a remittent low pyrexia, lasting fifty-two days and terminating on the aspiration of 10 ounces of clear fluid from the chest. In the initial attack there was abdominal discomfort, but no rose spots or obvious enlargement of the spleen.

Agglutination reactions were as follows:

Time after beginning of disease.	Typhoid.	Para A.	Para B.	Bacillus fecalis.
4½ months	500	100	20	40
5½ "	160	80	20	20

In the third case the temperature curve was typical of typhoid fever, the pyrexia continued for twenty-three days, falling by lysis. Diarrhea was present, but there were no rose spots or splenic enlargement. The pulse was dicrotic and temperature and pulse ratio was low, for example, temperature 104° F. and pulse 90.

Agglutination reactions were as follows:

Time after beginning of disease.	Typhoid.	Para A.	Para B.	Bacillus fecalis.	Own organism typhoid.
2½ months	1000	250	250		
3½ "	500	100	20	20	1000
4½ "	500	50	20	20	1000
5½ "	500	50	..	..	500

Bacillus typhosus was found uninterruptedly in the stools for seventy-six days. Bacillus fecalis alkaligenes was found once, eleven days after the Bacillus typhosus was last found.

The fourth case had fever for twelve days accompanied by diarrhea. The spleen was palpable on deep inspiration. There was slight jaundice. Clinically this case did not appear to have been typical of any specific disease.

The agglutinations, which were done three and a half months after the beginning of the disease, were as follows:

Bacillus fecalis (own organism).	Bacillus typhosus.	Para A.	Para B.
40	80	20	0

It would be interesting to know at what periods of the pyrexia of these 4 cases that the Bacillus fecalis and typhoid group organisms were obtained in the blood cultures. This was not stated. Since the sera of these patients showed such high agglutination with the typhoid group organisms and such low agglutination with Bacillus fecalis, it is not probable that the latter organism would be taken as the cause of the illness.

In September, 1923, Row[19] treated a patient whose general condition was that of typhoid fever. Bacillus typhosus was agglutinated in dilutions of 1 to 10 but not in the higher dilutions. Bacillus paratyphosus A, B and C were not agglutinated. Bacillus fecalis was obtained from the stools. The dilutions of the agglutinating reactions were not given and the laboratory reports are very ambiguous.

Etiology. The disease has been observed in Germany and France, but most of the cases reported have been in Egypt and oriental Asia. It may exist in a sporadic state or it may appear as an

epidemic. In Egypt it seems to be endemic. Rochaix and Blanchard[17] tabulated 37 of the undoubted cases and found it most common in spring and summer. It would seem from this that warm climates and warm seasons are a factor.

It is a disease of adolescents or of adults, and most of the cases have been observed in soldiers and sailors. Only 2 cases in women have been reported.

Overwork and fatigue seem to be etiologic factors. Shearman and Moorehead[20] have pointed out that "in climates, such as Egypt, where gastrointestinal disturbances are rife, especially among fresh troops who are exposed to unusual hardships before being acclimatized, the catarrhal condition of the bowel so set up provides a point of least resistance and the organism hitherto passive and harmless, now assumes an active part and invades the blood stream." Bacillary dysentery and the typhoids were frequent precedents in the cases reported from Egypt.

Fischer,[4] in 1899, found Bacillus fecalis alkaligenes in the canal water of Dantzig. The suburbs, which furnished nearly the total number of typhoidal affections of this city, disposed of their sewage in this canal. And Klimenko,[8] in 1907, discovered it in the canal waters of the school of the marines of Petrograd.

Hirst[7] states that several bacteriologists of Egypt have isolated it from the dust and water of that country.

Neufeld[13] recovered it in 1903 in the aqueous contents of a very inflamed small intestine of a person who had died with an acute choleriform enteritis.

From 1907 to 1911 Martini[11] isolated it in large numbers in the stools of 5 dysenteric cases and 2 enteritis cases and from the stools of 3 subjects who had lived with the precedents.

In the stools of 2 individuals ill with dysenteric affections D'Hérelle[3] found the Bacillus fecalis alkaligenes in the proportion of 96 to 100 of intestinal flora for the first case and 90 to 100 in the second case. No other pathogenic organisms were found.

As mentioned above, Webster[22] obtained it in blood cultures on 3 infants with acute enterocolitis.

Hirst[7] made a bacteriologic examination of the stools of healthy individuals and of those convalescing from typhoid and dysentery with the following results:

	No. of subjects.	Bacillus fecalis alkaligenes.
Convalescents from typhoid	45	16
Convalescents from dysentery	57	27
Healthy subjects	50	0

The infection undoubtedly is water-borne in most of the cases reported, but as in typhoid, food, fingers and flies may also be the means of spreading the disease. Bacillus fecalis is motile, Gram-negative, usually bipolar flagellation, although some strains show

unipolar and peritrichic, does not produce acid or gas on sugars, but does produce alkaline reaction; nonformation of H_2S and indol.

Lesbre and Vardeau[10] have shown that the various strains of Bacillus fecalis grow in media inoculated with Bacillus typhosus, Bacillus paratyphoid A and B, Bacillus of Shiga, Bacillus choleræ asiaticæ and Bacillus coli. However, none of these organisms grow in media inoculated with Bacillus fecalis. The authors point out that these characteristics agree with clinical observations, that Bacillus fecalis is an organism associated with typhoid, cholera and dysentery infections. They also state that the bacilli of the fluorescent group grow abundantly in media inoculated by Bacillus fecalis, without reciprocity.

Michaelis[12] had found that for each species of bacteria there was a specific optimum concentration of hydrogen ions which would produce the best agglutination. Lesbre and Vardeau[10] used his technique with their six strains of Bacillus fecalis, but they did not present a fixed and specific point of flocculation according to the conception of Michaelis.[12]

With the deviation of complement the authors showed the specific unity of Bacillus fecalis and differentiated it from the typhoid, paratyphoid and fluorescent bacilli. Their conclusion was that the species fecalis presented a greater homogeneity than the species coli.

Pathology. The only pathologic report of an undoubted case of Bacillus fecalis alkaligenes bacteremia is by Ravenel,[16] University of Missouri School of Medicine. His report, in brief, is as follows: Male, aged twenty-one years, died on sixth day of clinical illness. Necropsy, which revealed lesions typical of typhoid fever in early stage, was made two hours after death. The spleen was enormously enlarged, measuring 22.5 by 13.5 by 10 cm.; weight, 850 gm.; it was dark colored, firm and granular in texture. The splenic nodules were prominent. The liver was slightly enlarged and congested. Microscopic sections revealed extensive focal necrosis. The mesenteric glands were enormously enlarged and congested. Extensive hyperplasia was evident in microscopic sections. The lower ileum contained a considerable amount of free blood. Beginning 71 cm. above the ileocecal valve, and extending to the valve, 8 ulcers were found, in size from 1 by 1 cm. to 8 by 2 cm. Between these ulcers 59 elevated patches were counted, the surfaces of which were not yet ulcerated, though surface layer of some could be easily rubbed off, leaving typical ulcers. These elevations were enlarged solitary and agminate glands. In the large intestine 89 enlarged solitary follicles were counted, 11 of which were ulcerated. These were situated from 2 to 43 cm. below ileocecal valve. The ulcers were early in type, the edges slightly elevated above the central areas, giving the typical plateau formation. The centers were yellow, shading into golden brown. There was necrosis, apparently

superficial, though microscopic sections disclosed that it extended down to the muscularis. There was no hemorrhage about the ulcers, though injected vessels were visible on the surface. On section the ulcers showed a thin layer of yellow necrotic material over white nodule quite distinct from the more pink surrounding tissues. The nonulcerated patches were similar in structure.

Cultures were from the spleen and intestinal patches which gave abundant growth of a typical colon bacillus and a typhoid-like organism, the latter greatly predominating. The typhoid-like organism had all the cultural characteristics of Bacillus fecalis. Several strains of known typhoid sera failed to agglutinate this organism. The lesions were those of severe infection by Bacillus typhosus.

A severe pyelonephrosis of pregnancy followed by uterine infection, puerperal peritonitis and death was reported by Hamm.[6] The illness began with an enteritis due, the author thought, to having eaten spoiled food (beer, cheese, sausage). Though cultures from the amniotic fluid and navel blood could not be made, a large amount of pus and the Bacillus fecalis alkaligenes were present in the urine. The abdomen was greatly distended and tender, and from it about 3 liters of turbid, bright yellow fluid were obtained on puncture. The lochia were not foul, and no streptococci were found in the peritoneal fluid. The patient died with symptoms of peritonitis, but unfortunately there was no autopsy. Owing to the lack of blood cultures and agglutination reactions, this cannot be classed as an undoubted case of Bacillus fecalis bacteremia.

In the Lexington Clinic there has been 1 case of bilateral pyelonephrosis and nephrolithiasis in which the urine from each kidney gave a growth of Bacillus fecalis. A case of carcinoma of the head of the pancreas was encountered where the gall bladder was distended to twice its normal size and the aspirated thick, black bile produced a growth of Bacillus fecalis.

Symtomatology. From Fürth's[5] 6 cases, which appeared in two series, it would appear that the incubation period is about fifteen days.

The symptoms are those of a mild typhoid, but usually differing from it by a more abrupt onset. A few cases have been reported with gradual onset. The symptoms complained of are slight chill, severe headache, usually frontal but sometimes also felt in occipital region, anorexia, nausea, occasional vomiting and aching of limbs. Abdominal pains accompanied by constipation were frequently complained of, although several authors reported diarrhea to be present in their cases. When the latter is present the stools are very liquid, yellowish and serous. Rochaix and Blanchard[17] describe it as resembling the juice of a melon.

Lassitude is present; often profound. Night sweats may sometimes cause prostration. The lips are dry and the tongue also dry

and covered with a brownish coat. In the clinical picture given by Hirst[7] he notes that the toxic appearance is out of proportion to patient's symptoms, which are usually indefinite.

The initial fever varies between 101° to 105° F., and continues from two to five days. The temperature then drops by lysis to normal for two to five days, when a recrudescence appears. This period of fever lasts two to three days and is similar to the first and is accompanied by a return of the symptoms. Two to three recrudescences are common, although there are some cases which have had none.

Rose spots have been observed only in 1 case. The spleen is only slightly hypertrophied. The pulse is relatively slow, as compared to the temperature, and is usually under 100. Epistaxis has not been observed; neither have any nervous symptoms, such as delirium and coma.

Complications. Generally the disease progresses without complications. An intestinal hemorrhage was seen in 1 case by Lafforgue.[9] A myocarditis was observed by Fürth.[5] In 1 case Hirst[7] recorded a pleurisy with effusion from which he isolated Bacillus fecalis in pure culture. This author also noted an erythema nodosum in 1 case.

Diagnosis. Owing to the absence of definite characteristics and pathognomonic signs the clinical diagnosis is extremely difficult. The disease is to be differentiated from typhoid and paratyphoid, which it so closely resembles. Its generally abrupt onset differs from the typhoidal infections, as do the frequent relapses. The absence of rose spots and the less pronounced hypertrophy of the spleen are also points mentioned in differentiation. As is well known, rose spots, unless numerous, are very uncertain of identification. The diazo reaction, which is practically always positive in typhoid, is usually absent.

In the Mediterranean region Rochaix and Blanchard[17] think it may be confused with Malta fever on account of the numerous relapses.

The diagnosis can only be made definitely by blood culture and agglutination tests. The blood cultures, as in typhoid, must be taken during the early stages of the pyrexia.

Prognosis. The prognosis is good. Only 1 death in the series of 40 cases reported has occurred.

Prophylaxis. Prophylaxis employed should be the same as in typhoid. The organisms are excreted in the urine and feces and these should be disinfected.

Treatment. The disease, like typhoid fever, is self-limited and nothing we know of has any appreciable effect upon its course. Some anodyne for the aching pains which are very annoying, at times preventing sleep, should be given. Tepid sponges, should the fever be high, give considerable comfort. The diet should be that of typhoid fever.

Report of Case. A pupil nurse, single aged twenty-one years, complained of headache, pain in abdomen and fever; duration three days.

Past History. Jaundice at six years and typhoid at seven years of age. Three to four attacks of tonsillitis a year. A mild attack of influenza in 1919. Frequent "bilious attacks" during childhood which were relieved by calomel. Has been habitually constipated. Has never had any diarrhea or dysentery. In October 1925 the patient was given three doses of typhoid vaccine.

Present Illness. Patient had been on night duty almost a month and had felt as well as usual except for headache, which lasted about half an hour, on awakening each afternoon. Early in the evening of May 23, 1926, "ears began ringing and became blind." Felt dizzy and sat down for ten minutes when symptoms disappeared. Continued on duty but all night felt chilly and had to wear a wrap to be comfortable. At 6.30 A.M. on May 24, felt warm and on taking her temperature found it to be 103°. Remained in bed May 24 and 25 and the fever continued, ranging between 99.6° and 103°. Late in the afternoon of May 25 had dull aching pains in both flanks, lumbar region of back and frontal headache. Appetite and digestion seemed about as usual. Constipation, which has been habitual, continued and she had no stool except by taking a laxative or an enema. There were no dysuria, pollakiuria or polyuria.

No patients with typhoid fever, diarrhea, or dysentery were on the ward where she was nursing.

Physical Examination. May 25: Temperature, 104.6°; pulse, 112; respirations, 30. The patient seemed to be in pain. She was well-nourished and developed. Skin negative for rose spots or other eruption. Cervical glands size of beans and not tender. Tongue coated brown. Tonsils hypertrophied and crypts filled with caseous material. Thyroid, breasts, heart and lungs negative. Abdomen: soft, tenderness along cecum and descending colon; right kidney palpable and very tender. Splenic dullness not increased and edge not palpable. Liver dullness normal. She complained bitterly of cramping pains in upper right quadrant and right flank.

May 25: Catheterized urine: Acid, 1010; albumin, trace; few pus cells.

May 26: Catheterized urine: Acid, 1022; albumin trace, otherwise negative. Leukocytes, 9620; polymorphonuclear neutrophils, 68 per cent; transitionals, 2 per cent; lymphocytes, 24 per cent; large mononuclears, 4 per cent; eosinophils, 2 per cent. Highest temperature, 103°; pulse, 96. Pain in right upper quadrant.

May 27: Highest temperature 102.4°; pulse, 100. Blood culture produced growth of Bacillus fecalis alkaligenes.

May 28: Leukocytes, 9480. Highest temperature, 102.6°; pulse, 90.

May 29: Highest temperature, 102°.

May 31: Catheterized urine: neutral, 1025; albumin, trace; a few pus cells and a few red blood cells; stained sediment showed no bacteria; culture produced no growth.

June 1: Blood culture produced Bacillus fecalis alkaligenes.

June 2: Widal reactions: Bacillus typhosus, moderate agglutination, 1 to 50; Bacillus paratyphosus A, no agglutination; Bacillus paratyphosus B, no agglutination. Bacillus fecalis alkaligenes obtained from blood culture was agglutinated by patient's serum in dilutions 1 to 20. No other dilutions tried.

June 19: Spleen palpable today for first time.

June 20: Blood culture produced no growth at end of seventy-two hours. Bacillus fecalis obtained from previous blood cultures was accidentally destroyed.

June 22: Wassermann reaction negative.

June 23: Stool cultured on eosin-methylene blue and Endo's plates produced a number of colorless colonies of Bacillus fecalis alkaligenes, proven by fermentation tests.

June 26: Patient's serum (diluted 1 to 80) agglutinated a strain of Bacillus fecalis obtained from her stool. The typhoid and paratyphoid A and B stains showed no agglutination.

July 5: Spleen has been palpable until today.

July 10: Agglutination tests: No agglutination of typhoid and paratyphoid A and B organisms. Bacillus fecalis alkaligenes obtained from stool was agglutinated by patient's serum in dilutions 1 to 50. No agglutination at 1 to 100.

The fever continued for fifty-seven days, falling by lysis.

October 5: No Bacillus fecalis could be demonstrated from stool culture.

October 8: Bacillus fecalis from stool was agglutinated by homologous serum in dilutions up to 1 to 50.

The clinical picture was that of a mild typhoid. Recovery was without complications.

Conclusions. Bacillus fecalis alkaligenes may be the cause of local manifestations, such as pyelonephrosis and enteritis.

It may also be the causal organism of a bacteremia with clinical symptoms of typhoid fever, but with a more favorable prognosis (1 death in 40 cases).

Intestinal hemorrhage, myocarditis, pleurisy and so forth may occur as complications.

The diagnosis can only be made definitely by blood culture and agglutination tests.

The treatment is that of a mild case of typhoid fever.

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THE SPECIFIC THERAPY OF PNEUMOCOCCUS TYPE II PNEUMONIA.

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In spite of the seriousness of pneumococcus Type II pneumonia, little progress has been made in developing a satisfactory specific therapy for it. Cole and his coworkers[1] at the Hospital of the Rockefeller Institute found that pneumococcus Type II was the etiologic agent in 31 per cent of all pneumococcus pneumonias, and that this group had a mortality rate of 32 per cent. Cecil, Baldwin, and Larsen,[2] as a result of their investigation of 1913 pneumococcus pneumonias at Bellevue Hospital, found pneumococcus Type II in 19 per cent of the series. The death rate in their series of 364 cases was 39 per cent.

Efforts at specific therapy in pneumococcus Type II pneumonia with Type II antipneumococcus serum or its derivatives have not been impressive. Avery, Chickering, Cole, and Dochez, as a result of their work at the Hospital of the Rockefeller Institute, concluded that pneumococcus Type II serum was much less efficacious than Type I serum, and stated that it had not been thoroughly demonstrated that it possessed any noteworthy effect on the outcome of the disease. Cecil and Larsen,[3] using the polyvalent antibody solution of Huntoon,[4] treated 83 cases of pneumococcus Type II pneumonia with a death rate of 27.7 per cent. In 65 control cases, the death rate was 40.3 per cent. These figures, while not brilliant, were suggestive as to the possibilities of a potent Type II serum.

Any attempt to treat pneumococcus Type II pneumonia with immune serum has to take into account the relative frequency of

pneumococcus septicemia in Type II pneumonia. Cole and his associates found a bacteremia at some stage of the disease in 33.1 per cent of their cases of pneumococcus Type II pneumonia. In those cases with bacteremia, the mortality was 73.4 per cent. Cecil, Baldwin and Larsen, were able to demonstrate bacteremia in 43.3 per cent of their cases of pneumococcus Type II pneumonia, and among these cases, the mortality was 90.3 per cent. On the other hand, a comparatively low mortality was noted in those cases in which bacteremia did not develop. At the Hospital of the Rockefeller Institute, only 9 per cent of the pneumococcus Type II cases with sterile blood culture died. At Bellevue Hospital the mortality in this group was 16.2 per cent. It is evident, therefore, that specific therapy in pneumococcus Type II pneumonia will be successful only when it is effective in preventing the development of bacteremia, or in sterilizing the blood when bacteremia has occurred.

The development of bacteremia during the course of pneumonia and its relation to the immune substances which develop in the serum during the course of the disease, has recently been studied in detail by Baldwin and Rhoades.[5] The amount of immune substance in the blood of patients was determined by measuring the protective value of the patient's serum. By protective value of serum is meant the capacity of pneumococcus immune serum to protect a mouse from death when injected intraperitoneally with lethal doses of homologous pneumococci. The substance present in immune serum which possesses this power is called protective substance. By taking blood from pneumonic patients daily and testing it for bacteremia and protective substances, Baldwin and Rhoades obtained evidence which indicated that bacteremia develops in the absence of sufficient protective substance. Furthermore, the development of an excess of protective substance during the course of pneumococcus pneumonia is apparently associated with recovery; when the amount developed is insufficient, the patient dies.

The potency of immune sera used in the treatment of patients with pneumonia is measured by its content of protective substance. In the case of pneumococcus Type II immune serum, it has not been possible until quite recently to secure a serum of high protective value. To quote from Cole,[6] "whereas the horse serum against Type I infection is of such a strength that 0.2 cc. will regularly protect a mouse against 0.1 cc. of virulent culture, it has been impossible to produce an immune Type II serum of any greater activity than 0.2 cc. will protect a mouse against 0.01 cc. of culture."

During the winter of 1925–1926, Dr. William H. Park,* of the

* The method of immunization used was the standard method of the New York City Board of Health. The high titer of the serum obtained was probably due to the unusual response of the horse inoculated. (Verbal communication from Dr. William H. Park.)

New York City Board of Health, immunized a horse with pneumococcus Type II, and obtained a serum of sufficient potency that 0.2 cc. would protect a mouse against 0.2 cc. of pneumococcus Type II virulent culture. We were able to use this serum in the treatment of Type II pneumonia at Bellevue Hospital during the winter of 1925–1926. Several of the protocols which follow illustrate the effect of its administration clinically, and on such purely objective findings as bacteremia and the appearance of protective substance in the circulating blood. In a few cases the pneumonoccus Type II concentrate of Felton[7] was used.

The investigation was carried on primarily to determine the requisites of successful specific therapy in pneumococcus Type II pneumonia from two standpoints: (1) The specific agent employed, and (2) the type of case suitable for therapy. In the protocols which follow it will be shown that by using pneumococcus Type II immune serum of sufficient potency, a balance of protective substance can be conferred and favorable clinical effects obtained in certain cases. Evidence will be given to show that following its administration a bacteremia of limited degree can be checked with recovery of the patient. On the other hand, the failure of specific therapy in heavy bacteremia or in severe toxemia will also be shown, and the relation of successful treatment to the duration of the disease, preceding its administration, will be discussed.

In the figures which follow, the upper solid line indicates the temperature, the lower solid line the number of pneumococci per 1 cc. of circulating blood. The broken line indicates the amount of protective substance in the blood expressed in terms of the number of lethal doses survived by mice. The small arrows at the top show the time and dosage of serum antibody injections.

The protection tests on mice were carried out according to the method used by Baldwin and Rhoades in the work already mentioned. The blood culture method used was the following: Beef infusion broth and blood agar plates were used for the cultures, 2 cc. of blood was drawn from the patient's arm, 1 cc. was added to the plain broth, the other cubic centimeter plated out in agar.

The following case of pneumococcus Type II pneumonia illustrates the natural production of a protective balance in the blood, prior to specific therapy, and its increase following the administration of Type II immune serum.

Case Reports. CASE I (Fig. 1).—W. B., male aged twenty-three years, a sailor, was admitted to the hospital on the second day of his illness. Early signs of consolidation were present in the left lower lobe. A blood culture taken on the fourth day of his illness was sterile. Blood was also taken (at the same time) for protection tests, before any immune serum had been administered. Protective bodies in an amount sufficient to protect a mouse against 100 M. L. D. of pneumococcus II culture were demonstrated. A few minutes after the blood had been withdrawn for culture and protection tests, the patient received 70 cc. of pneumococcus Type II

immune serum intravenously. Five hours after the administration of the pneumococcus Type II serum, the protective power of the blood had increased so that it protected against 10,000 M. L. D. of pneumococcus II culture. During the following twenty-four hours, three more injections of pneumococcus Type II immune serum were given (80 cc., 120 cc., and 50 cc.). On the fifth day of the disease, the temperature had fallen slightly, and the balance of protective substance in the blood was still high. On the sixth day, crisis occurred, and the patient made an uneventful recovery. Blood cultures were sterile throughout.

The next 4 cases illustrate the first appearance of a protective balance in the blood of patients with pneumococcus Type II pneumonia following

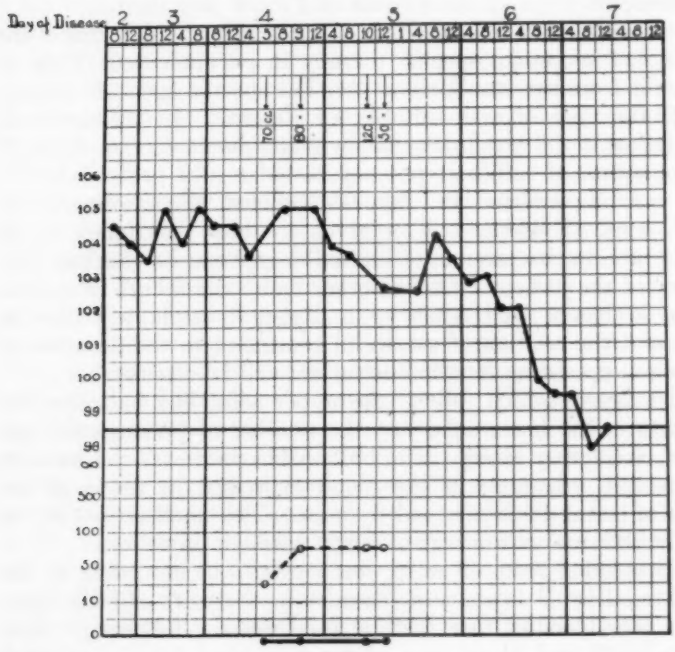

FIG. 1. (Case I).—Pneumococcus Type II pneumonia. Pneumococcus Type II protective substance in blood on fourth day of disease preceding administration of pneumococcus Type II immune serum; increase in amount of protective substance following immune serum. Blood cultures sterile.

the administration of protective substance in the form of pneumococcus Type II immune serum. In these cases no bacteremia was demonstrable before treatment or at any time during the subsequent course.

CASE II (Fig. 2).—S. F., male, aged thirty-five years, was admitted to the hospital on the second day of his illness. Physical examination showed consolidation in the right upper lobe. On the third day of his illness at 12 o'clock noon, blood cultures were sterile and no protective substance was demonstrable in the serum. A few minutes after taking the patient's blood, 50 cc. of pneumococcus Type II immune serum was given intravenously. Four hours later, another 50 cc. of serum was given. At the time of the second injection of serum, the blood was sterile, and instead of showing

no protection, as it had previous to the first injection, it now contained sufficient protective substance to protect against 100,000 M. L. D. of pneumococcus Type II culture. Two more injections of pneumococcus Type II immune serum, consisting of 50 cc. each, were given on the fourth day. The temperature subsided by lysis in a way that suggested a possible therapeutic effect from the administration of the serum. A leukocyte count taken on the third day showed 27,000, 95 per cent polymorphonuclears.

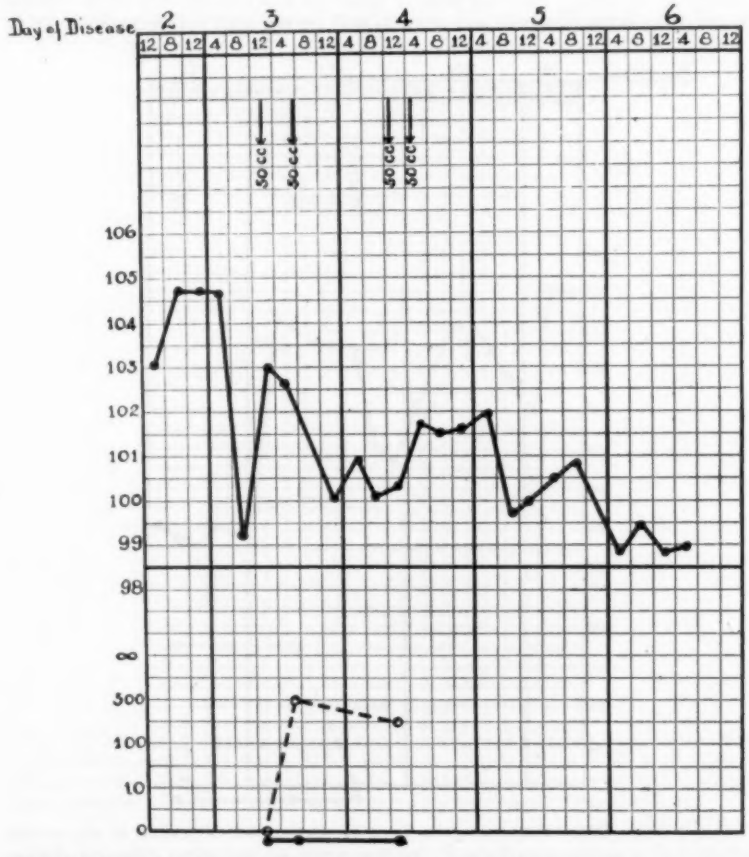

FIG. 2 (Case II).—Pneumococcus Type II pneumonia; 50 cc. of pneumococcus Type II immune serum given on the third day of illness. Before serum administration no protective substance in blood; four hours later, considerable protective balance demonstrable. Blood culture sterile. Lysis on sixth day. Illustrates the appearance of a protective balance in the blood following the administration of 50 cc. of Type II immune serum.

CASE III (Fig. 3).—J. G., male, aged forty-nine years, was admitted to the hospital on the ninth day of his illness. Frank signs of consolidation were found in the right upper and middle lobes. On the eleventh day, with the patient delirious, markedly cyanotic, and giving every appearance of soon becoming moribund, blood was withdrawn for culture

and protection tests. The blood culture was sterile, but no protective substance was present. Three injections of pneumococcus Type II immune serum, each consisting of 70 cc., were given intravenously at two-hour intervals. Two hours following the third injection, a fourth was given, blood being taken previously for culture and protective substance. At this time, the blood was still sterile, and the serum now showed protective power sufficient to protect against 1,000,000 M. L. D. of pneumococcus Type II culture. Twelve hours following the institution of treatment, crisis had occurred, and the patient made an uneventful recovery. White blood cells on the eleventh day were 24,000, 89 per cent polymorphonuclears.

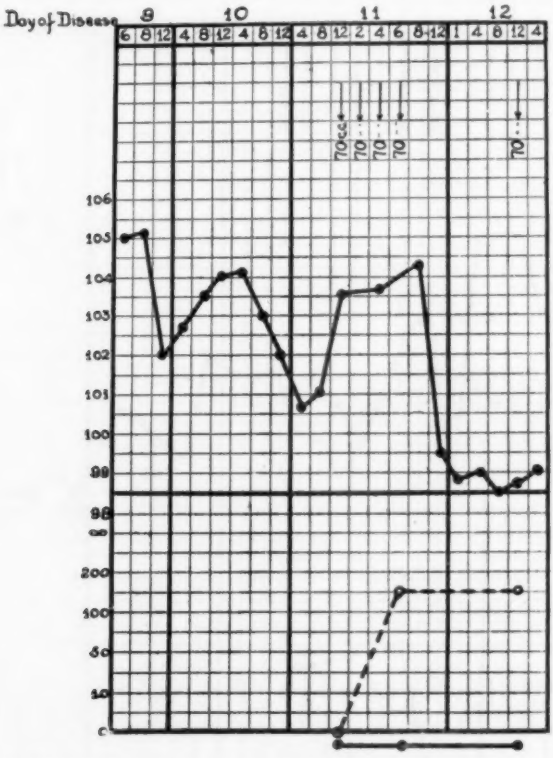

FIG. 3 (Case III).—Pneumococcus Type II pneumonia. Previous to the administration of pneumococcus Type II immune serum no protective substance demonstrable in blood. Following administration of 210 cc. of Type II immune serum considerable amount of protective substance present in blood. Crisis twelve hours following the institution of treatment. Blood cultures sterile.

This case again illustrates the presence of considerable protective substance in the blood following administration of Type II immune serum. The blood culture remained sterile, and the close succession of crisis to treatment in a very severely ill patient suggested a therapeutic effect.

CASE IV (Fig. 4).—W. S., male, aged twenty-nine years, was admitted to the hospital on the second day of his illness, with signs of consolidation in the right lower lobe. A Krumwiede test showed pneumococcus Type

II in the sputum. At 11 A.M., on the third day, blood was taken for culture and for protection tests. The first specimen of blood was found to be sterile, and to contain no protective substance. Almost immediately after withdrawal of the blood, the patient received 70 cc. of Type II immune serum intravenously. Two hours later, blood was again withdrawn for culture and protection tests. At this time, an amount of protective substance sufficient to protect against 1000 M. L. D. of Type II culture was demonstrable in the patient's blood. Following this bleeding, the patient received 140 cc. of Type II antipneumococcus serum. At 5 P.M., or six hours after the first injection of serum, the patient's serum continued to show protection *vs.* 1000 M. L. D. of pneumococcus Type II culture.

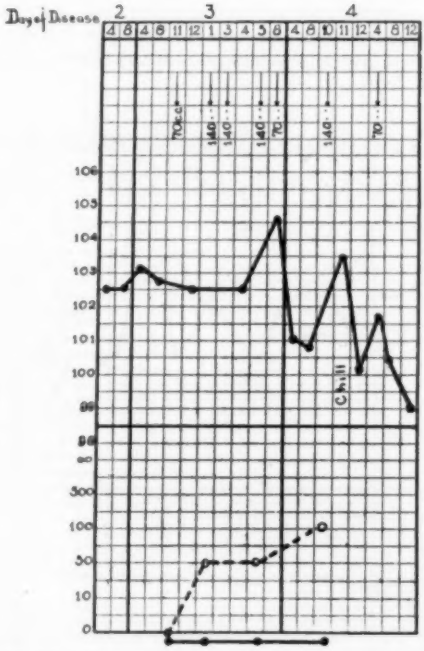

FIG. 4 (Case IV).—Pneumococcus Type II pneumonia showing early appearance of protective substance in the blood following the administration of 70 cc. of Type II immune serum. The amount of protective substance increased with further serum administration. Lysis on fourth day. Blood cultures sterile throughout.

At this time, the very serious condition of the patient induced us to administer still more serum (210 cc.). The following morning, on the fourth day the temperature had dropped to 101°. A further dose of 140 cc. was given. This was followed by a mild chill, the temperature rising to 103.5°. Following the chill, the temperature dropped to 100°, and then quickly rose to 101.7°. An injection of 70 cc. of pneumococcus Type II immune serum, at this time, was followed by a drop of temperature to normal. The blood culture remained sterile, and the protective power of the serum on the day when lysis took place was sufficient to protect against 100,000 M. L. D.

In this case, large doses of pneumococcus Type II immune serum were given. Seventy cubic centimeters of immune serum served to produce a

balance of protective substance in the blood. The temperature subsided to normal on the fourth day, an unusual occurrence in Type II pneumonia.

CASE V (Fig. 5).—C. Anderson, male, aged nineteen years, was admitted to the hospital on the second day of his illness with signs of consolidation in the left lower lobe. On the third day of his illness 4 cc. of a concentrated Type II immune serum of Felton was given, but as this was followed immediately by cyanosis and severe headache, its administration was discontinued. A blood culture at this time was sterile and no protective substance was demonstrable in the patient's serum. On the fourth day at 12 noon, 70 cc. of Type II antipneumococcus serum was given. A blood culture at this time was still sterile and no protective substance was demonstrable. Four hours later, however, considerable protective substance was present. With continued administration of immune serum, the blood culture remained sterile, the protective balance was increased and the patient's fever resolved by lysis on the ninth day.

FIG. 5 (Case V).—Pneumococcus Type II pneumonia showing the rapid appearance of protective substance in the blood following the administration of 70 cc. of immune serum. With the continuation of serum therapy a protective balance was maintained in the blood. In spite of this, however, no demonstrable effect on the temperature curve occurred. Blood cultures sterile.

This case again illustrates the rapid appearance of protective substance in the blood following the administration of Type II antipneumococcus serum. The blood culture remained sterile throughout. It is interesting to note that in this case serum treatment and the early appearance of protective substance in the blood of the patient failed to shorten the course of the disease. Baldwin and Rhoades have shown that in nearly 50 per cent of untreated pneumonic patients the natural protective substance appeared two days or more before the day of crisis or lysis. Patients with pneumonia may exhibit a considerable degree of toxemia even when a high degree of protective substance is present in the blood.

The next three are cases in which the blood culture was positive before the administration of serum, but became negative after serum treatment.

CASE VI (Fig. 6).—G. P., male aged fifty years, was admitted to the hospital on the second day of his illness. Physical examination showed early signs of consolidation in the left upper and left lower lobes. Blood culture taken on the third day before the administration of serum showed five colonies of pneumococcus Type II per cc. of blood, and no protective substance was demonstrable. At 4 P.M. on the same day, immediately following the blood culture, patient received 50 cc. of Type II serum intravenously. The following morning, the blood culture was sterile, and at this time, the patient's serum had a small amount of protective sub-

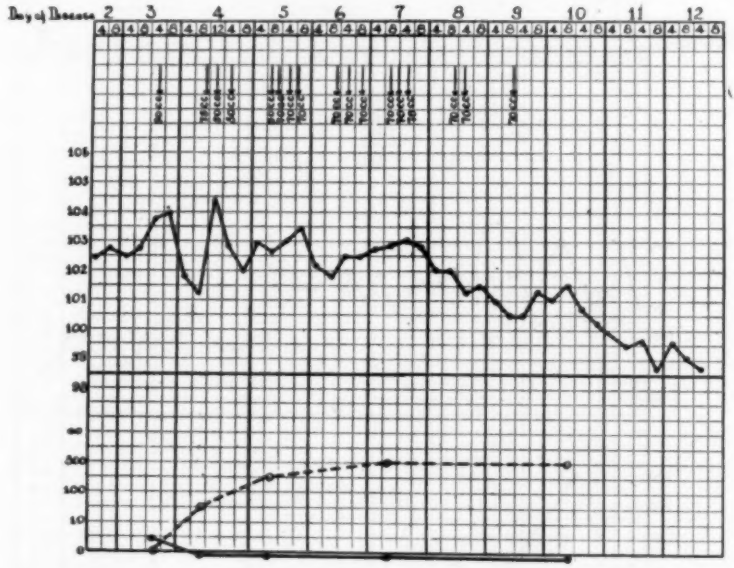

FIG. 6 (Case VI).—Pneumococcus Type II pneumonia with bacteremia consisting of five colonies per cc. on the third day of the disease. Previous to the administration of 50 cc. of pneumococcus Type II immune serum no protective substance demonstrable in blood; following its administration, the blood culture became sterile and a protective balance was established. With continuance of serum therapy, amount of protective substance increased. Blood culture remained sterile. Lysis on the eleventh day.

stance—enough to protect against 100 M. L. D. of pneumococcus Type II culture. Serum therapy was continued during the following five days. The blood culture remained sterile and the protective balance in the blood increased. Recovery took place by lysis on the eleventh day.

This case illustrates the rare recovery of a case of pneumococcus Type II pneumonia with bacteremia. Following the administration of a pneumococcus Type II immune serum of high potency, the blood became sterile and a protective balance was achieved early in the disease. With the continuance of serum therapy, the protective balance was increased, and the blood remained sterile. This case, with only a few colonies in the blood stream early in the course of the disease, illustrates the type of Type II bacteremia that may recover without specific serum. In the

statistics of the Rockefeller Institute study reported by Cole and his associates, only the cases of Type II bacteremia consisting of less than 15 colonies per cubic centimeter of blood ever recovered. Even in this latter group, the mortality was 44.4 per cent. It will be noted that, in this case, in spite of the large amount of circulating protective substance, very little effect on the temperature curve was demonstrable. Lysis did not occur until five days after a definite protective balance had appeared.

CASE VII (Fig. 7).—J. R., male, aged twenty years, was admitted to the hospital on the first day of his illness. Physical examination showed a small patch of consolidation in the left lower lobe. On the second day of the disease, the patient's blood contained 250 colonies of Pneumococcus II per cubic centimeter of blood. Following the intravenous injection of

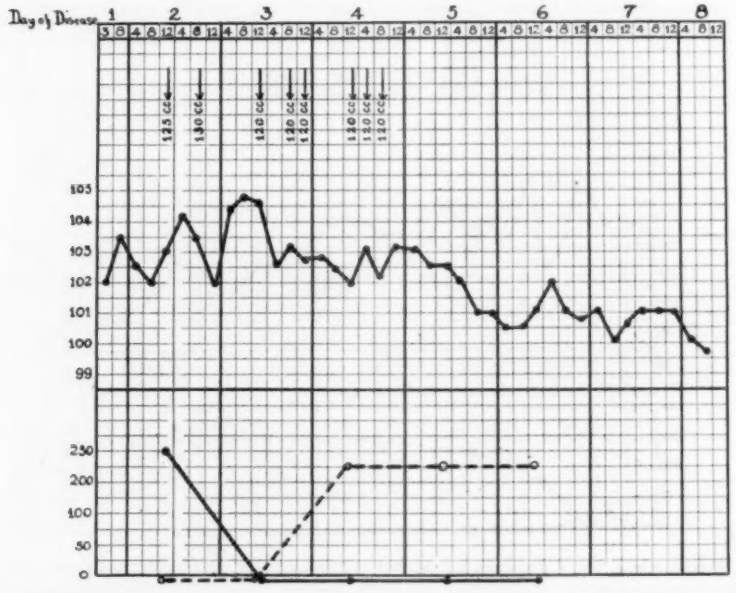

FIG. 7 (Case VII).—Pneumococcus Type II pneumonia showing the disappearance of pneumococci from the blood stream following 255 cc. of Type II immune serum. Further serum administration resulted in the establishment of a protective balance in the blood. Lysis on eighth day.

255 cc. of pneumococcus Type II immune serum, the blood became sterile. No Type II protective substance, however, could be found in the blood stream on the third day. On the fourth day, after receiving 360 cc. of immune serum intravenously, the blood showed protective power to a marked degree. This balance of protective substance persisted, the blood culture remained sterile, and the fever subsided by lysis.

In this case, a severe Type II bacteremia disappeared following the administration of pneumococcus Type II immune serum. Apparently, however, the protective substance administered on the first day while sufficient to clear the blood of pneumococci, was not sufficient to provide a positive balance of immune bodies in the blood until after the second day of specific treatment. The third day of the patient's illness represented a very critical one in his course. Until larger amounts of immune serum had

been administered, it was quite possible that pneumococci would reappear in the blood and a fatal septicemia supervene.

CASE VIII (Fig. 8).—E. G., male, aged twenty years, was admitted to the hospital on the second day of his illness. Frank signs of consolidation were present in the right lower lobe. On the third day at 12 noon, the patient had five colonies of pneumococcus Type II per cubic centimeter of blood. No protective substance was present. At 5 P.M., following the administration of 205 cc. intravenously of Type II immune serum, the blood culture was sterile, and a large amount of protective substance,

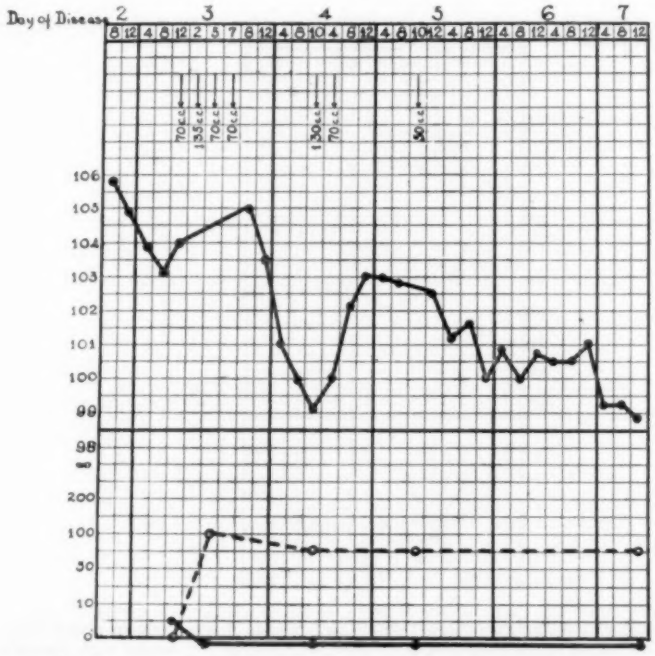

FIG. 8 (Case VIII).—Pneumococcus Type II pneumonia with bacteremia on the third day of illness. Following the administration of 205 cc. of pneumococcus Type II immune serum the pneumococci disappeared from the blood stream. Considerable protective substance was demonstrable. Blood culture remained sterile. Lysis on sixth day.

sufficient to protect against 100,000 M. L. D. was present. On the fourth day, the patient apparently had a crisis. Treatment was continued, however. In the afternoon, the temperature rose to 103°. The following morning, a few râles were heard in the left lower lobe, and the rise in fever was attributed to a small patch of consolidation in this lobe. The temperature subsided by lysis, and reached normal on the seventh day.

This case also illustrates the rapid disappearance of pneumococci from the blood following the administration of immune serum. A protective balance was established within five hours following the first injection of serum. Such an occurrence in so short a time and so early in the disease is difficult to explain, except as a result of the immune serum.

The following four charts illustrate the failure of the administration of immune serum in Type II pneumonia with bacteremia.

CASE IX (Fig. 9).—T. A., male, negro, aged fifty years, admitted to the hospital on the seventh day of his illness. A Krumwiede test of the sputum showed pneumococcus Type II. The patient was admitted with delirium tremens, and at the time treatment was instituted, pulmonary edema had already appeared. At 10.30 A.M., on the eight day of his illness, the blood culture was positive for pneumococcus Type II, and no protective substance was present. Seven hours later, following the administration of 65 cc. of Felton's concentrated Type II serum, the blood culture was sterile and a

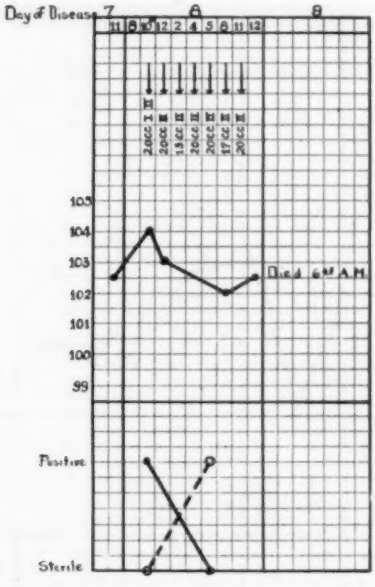

FIG. 9 (Case IX).—Pneumococcus Type II pneumonia; bacteremia on eighth day. Patient in beginning pulmonary edema at time of admission. Treated with Felton's concentrated Type II antibody solution. Following the administration of 65 cc. of pneumococcus Type II concentrate blood culture cleared and protective balance was established. In spite of this patient died. Autopsy showed every lobe in complete or partial consolidation. Illustrates the failure of specific therapy late in course of disease.

large amount of protective substance was present. The patient became steadily worse and died on the morning of the ninth day. Autopsy showed consolidation of every lobe.

This chart is shown to emphasize the failure of specific therapy when administered late in the course of the disease to a patient already severely injured by previous toxemia and spread of the infection. The case also illustrates the poor prognosis associated with chronic alcoholism and delirium tremens. Specific therapy in this case provided a balance of protective substance in the blood, and sterilized the blood. To this extent, it fulfilled its function. It could not, however, undo the deleterious effects of prolonged toxemia and septicemia.

CASE X (Fig. 10).—M. M., male, aged forty-nine years, admitted to the hospital on the second day of his illness. Physical examination showed consolidation of the right upper lobe. On the third day of his illness, a blood culture showed 12 colonies of pneumococcus Type II per cubic centimeter of blood and no protective bodies. Ten cubic centimeters of Felton's concentrated Type II serum was administered intravenously at noon on the same day. On the fourth day, the blood showed 200 colonies of pneumococcus Type II per cubic centimeter of blood and still no protective substance. On the fourth day, 350 cc. of Type II immune serum was administered. On the following morning (the fifth day) the number of colonies per cubic centimeter of circulating blood had fallen to 5 colonies per cubic centimeter. No protective substance was demonstrable at this

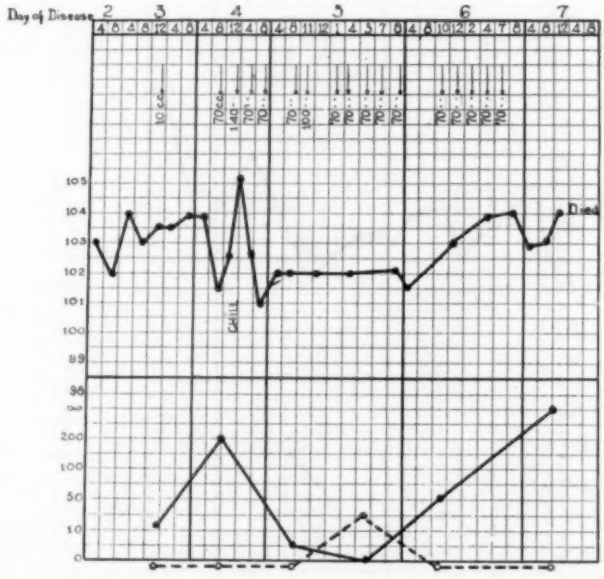

FIG. 10 (Case X).—Pneumococcus Type II pneumonia; illustrates the failure of specific therapy that is often encountered when it is started in the presence of a heavy bacteremia. Although the blood culture became sterile and a small protective balance was established it was impossible to maintain this status and patient died on the seventh day.

time. At 5 P.M., following the administration of 310 cc. of pneumococcus Type II immune serum during the day, the blood culture was sterile, and sufficient protective substance was present to protect against 100 M. L. D. of pneumococcus Type II culture, 210 cc. of serum were then given. The following morning (the sixth day), the blood culture was again positive; this time showing 50 colonies per cubic centimeter. Five injections of 70 cc. each were given during the day. Larger amounts of serum were not given at one time because of the fact that a previous injection of 140 cc. had been followed by a severe chill and the patient's condition was considered too serious to risk a similar reaction. On the morning of the seventh day, the number of pneumococci in the circulating blood were too numerous for estimation. The patient at this time had a stiff neck, positive Kernig's sign, and was wildly delirious. Death occurred shortly after.

No autopsy was obtained, but no further increase in the amount of consolidation other than the involvement of the right upper lobe could be found clinically. Leukocyte count on the day of death showed 4000 cells, 95 per cent polymorphonuclears.

In this case, specific therapy produced a sterilization of the patient's blood and a balance of protective substance in his serum, but the effect was only temporary. Here again, intensive serum treatment was started too late. The almost negligible amount of serum given on the third day had no effect, and by the fourth day, the blood contained 200 colonies of pneumococci per cubic centimeter.

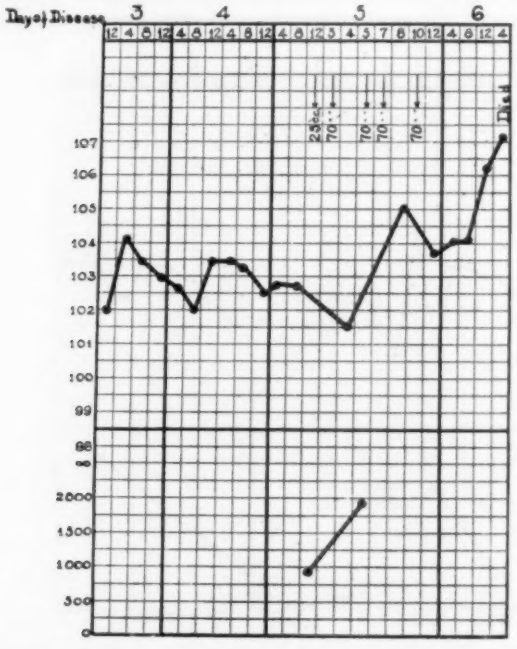

FIG. 11 (Case XI).—Pneumococcus Type II pneumonia with bacteremia; illustrates the failure of pneumococcus Type II serum when given relatively late in the course of the disease and in the presence of a heavy bacteremia.

CASE XI (Fig. 11).—H. M. M., aged twenty-four years, admitted to the hospital on the third day of his illness. Frank signs of consolidation in the right lower lobe. The patient was a chronic heroin addict, taking 1 gm. a day. On the fourth day of his illness, the left lower lobe became involved. On the fifth day, the blood culture showed about 1000 colonies of Pneumococcus II per cubic centimeter. Five hours later, in spite of the injection of 95 cc. of pneumococcus Type II immune serum, the number of pneumococci per cubic centimeter had doubled. The patient died the following day.

This case illustrates the failure of pneumococcus Type II serum to overcome a very heavy septicemia.

CASE XII (Fig. 12).—D. McS., male, aged twenty-four years, admitted to the hospital on the third day of his illness. Previous health good.

Frank signs of consolidation in the left lower lobe. Treatment was commenced on the third day, using Felton's concentrated Type II immune serum intravenously. At the start of treatment, a bacteremia was present, consisting of 4 colonies of Pneumococcus II per cubic centimeter. After 20 cc., the blood culture was sterile, but no protective substance was demonstrable. Treatment was continued on the fourth, fifth and sixth day with small amounts of the concentrate. In spite of the serum, bacteremia became progressively more marked, and the patient died on the sixth day of his illness. At no time during the patient's illness did the blood show a balance of protective bodies. White blood cell count on the fifth day showed 4000 cells. Autopsy showed consolidation of the left lower lobe and a collection of yellow serous fluid in the left chest.

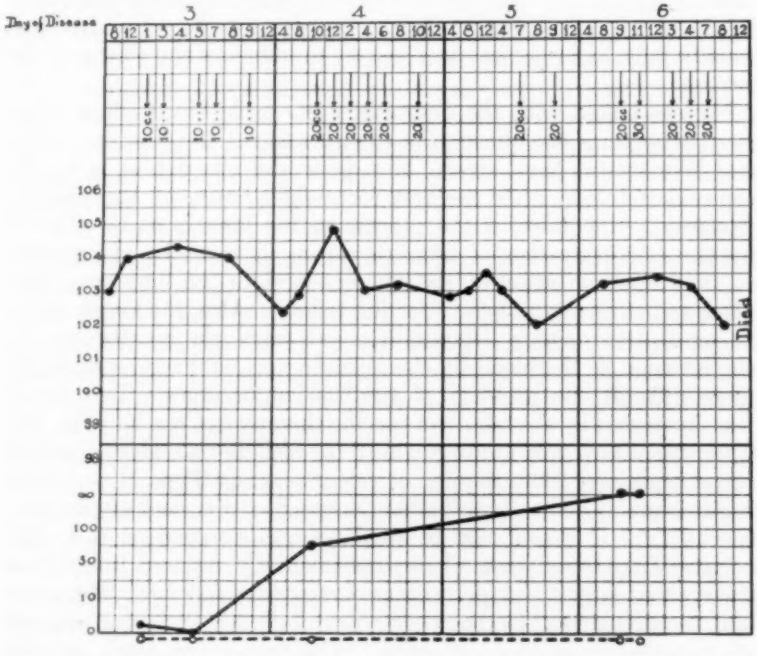

FIG. 12 (Case XII).—Pneumococcus Type II pneumonia. Treatment with Felton's concentrated Type II solution started early and in the presence of a light bacteremia. Illustrates the handicap of being unable to give sufficient antibody solution due to the possibility of severe chill reaction. Bacteremia increased. Death on sixth day.

This case is shown to illustrate the failure of specific therapy in a pneumococcus Type II pneumonia with bacteremia and to stress some of the difficulties which are encountered in the administration of serum derivatives at the present time. The case was treated relatively early, at a time when only a few pneumococci were present in the circulating blood. Because of the severe chill reactions which often follow the administration of these derivatives intravenously, only relatively small amounts could be given. In this case, it was possible to sterilize the blood, yet a protective balance could not be produced. It is conceivable that, had it been possible to give this patient doses of 100 to 200 cc. of the concentrate early in the disease,

a reserve of protective substance could have been produced and further invasion of the blood stream by the pneumococcus prevented.

Discussion. The frequent intravenous injection of 50 to 100 cc. of a pneumococcus Type II immune serum, of such potency that 0.2 cc. will protect a mouse against 0.2 cc. of a highly virulent Pneumococcus II culture, will nearly always confer a balance of protective substance on the patient's blood and favor recovery in cases where the blood culture is sterile. In the same way, injections of such serum in the case of a Pneumococcus II bacteremia of slight extent may sterilize the blood and provide more favorable conditions for recovery. In cases of heavy bacteremia, its administration usually fails, as far as we can observe, to influence the course of the disease.

Closely linked with the desirability of sterile blood when treatment is begun is the question of the duration of the disease. Kline and Winternitz[8] have shown how poor the circulation is in the consolidated lobe after the first forty-eight hours of the disease. Apparently therefore, if the process in the lung is to be aborted by the administration of immune serum, it must be given early so that opsoninization of the pneumococci in the lung may take place and subsidence of the infection follow. Also, the longer specific serum treatment is delayed in severe cases, the greater may be the invasion of the blood by the pneumococci, and correspondingly more difficult the problem of sterilization becomes. This factor was illustrated by the failure of specific therapy in Case XI (Fig. 11), where treatment was not begun until the fifth day, at which time the blood contained 1000 colonies of pneumococcus Type II per cubic centimeter. Cecil and Steffen[9] in the specific treatment of pneumococcus Type II pneumonia in monkeys also experienced this difficulty. They found that when experimentally induced pneumonia was treated early a high percentage of recoveries followed. If treated late, the circulating blood was overwhelmingly septic, and no amount of immune serum was effective. The important work on the soluble substance by Cole,[6] Dochez[10] and Avery and Heidelberger[11] points to the fact that in severe cases the development of soluble substance may be so great late in the disease that it is impossible to neutralize it with immune serum.

Finally, the aim in the specific treatment of any case of pneumococcus pneumonia is to prevent or check pneumococcus bacteremia and establish a balance of protective substance in the patient's blood. Baldwin and Rhoades have shown that bacteremia apparently develops in the absence of sufficient protective substance. The work of Bull[12] in treating septicemia in rabbits is confirmatory of this. He showed that in cases of pneumococcus septicemia in rabbits, the administration of immune serum provided for the agglutination and final phagocytosis of circulating pneumococci

and subsequent sterilization of the blood. Serum treatment, by conferring an artificial protective balance, may prevent bacteremia and allow the individual to rally his own immune mechanism into action.

In some cases of pneumococcus pneumonia, regardless of the time of treatment, or presence or absence of bacteremia, specific treatment fails to exert any favorable influence. In pneumococcus Type II infections, one should be sure that the organism is not an atypical Type II, for which the immune serum is not highly specific. Some individuals are so affected by the toxemia of the disease that their own immune mechanism never becomes very effective. This may have been the reason for the failure to achieve ultimate recovery in patient Case X, Fig. 10. Failure of resolution to take place in the consolidated lobe through the usual enzymatic action may be and probably is another factor. Of course, the influence of old age and chronic systemic disease is very important in its bearing both upon the patient's resistance to toxemia or production of antibodies.

As a result of this investigation, it appears that the successful specific therapy of pneumococcus Type II pneumonia is largely dependent upon the use of a highly potent serum in large amounts early in the course of the disease. A serum of the potency of that used in this work is not at present widely available. Concentrated Pneumococcus II immune serum derivatives may be very helpful if they can be administered in adequate amounts without causing severe chill reactions.

Conclusions. 1. Death in pneumococcus Type II pneumonia usually occurs in patients that develop pneumococcus bacteremia.

2. Patients with pneumococcus Type II pneumonia whose blood remains sterile usually recover.

3. With a highly potent Type II antipneumococcus serum it is possible to sterilize the blood in a certain number of cases of Type II pneumonia.

4. In pneumococcus Type II pneumonia with bacteremia, sterilization of the blood is most frequently effected when Type II serum is administered early in the disease. At this time the number of pneumococci in the blood is usually small. In early cases, where pneumococci have not yet invaded the blood stream, the administration of Type II serum may establish a balance of protective bodies in the blood and thereby lessen the chances of a subsequent pneumococcus bacteremia.

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BALLOONING OF THE LEFT LOWER ABDOMINAL QUADRANT AS AN EARLY SIGN IN PERFORATED DUODENAL ULCER.

(With Observations on the Characteristic Spread of Rigidity in Acute Abdominal Lesions).

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NEW YORK CITY.

A recent experience has induced me to place the following observation on record in the hope of contributing something toward the early recognition of perforated duodenal ulcer, and of possibly preventing a diagnostic error which might result from an incorrect interpretation of the symptom noted.

H. C., male, aged forty-seven years, developed a sudden acute abdominal pain with vomiting. His bowels had not moved for two days, and a high enema produced no result. Two hours after the onset of his symptoms a very careful medical man observed a marked distention of the left lower abdominal quadrant, presumably produced by a dilated intestinal loop. He thought he had also observed visible peristalsis. He suspected an intestinal obstruction, probably due to a volvulus of the sigmoid. This impression was shared by another very keen medical colleague, and the case was seen by me about four hours after the initial symptom. On taking the history it was found that the patient had been a chronic sufferer from hyperacidity and vague gastric disturbances for many years. On examination the most striking feature was, to be sure, a very pronounced ballooning of the left lower abdominal quadrant, the balance of the abdomen seeming very flat by comparison. No visible peristalsis could be detected and, on palpation of this region, it was found soft and insensitive. On the other hand, in the right upper abdominal quadrant there was boardlike rigidity, exquisite sensitiveness and marked rebound tenderness. In the right lower quadrant a similar condition existed to a somewhat lesser degree, and in the left upper quadrant there was also rigidity, sensitiveness and rebound tenderness, but still less than in the right lower quadrant (Fig. 1). The liver dullness, though not entirely obliterated, was distinctly dimin-

ished. On the basis of the history and findings, in spite of the definite ballooning of the left lower quadrant, a diagnosis of perforated duodenal or possibly pyloric ulcer was made, and at operation a large perforation in the anterior wall of the first portion of the duodenum was found as anticipated, with an extravasation of the duodenal contents in the right upper, right lower and left upper abdominal quadrants. As prophesied, during the anesthesia, when the abdominal muscles relaxed, the ballooning of the left lower quadrant

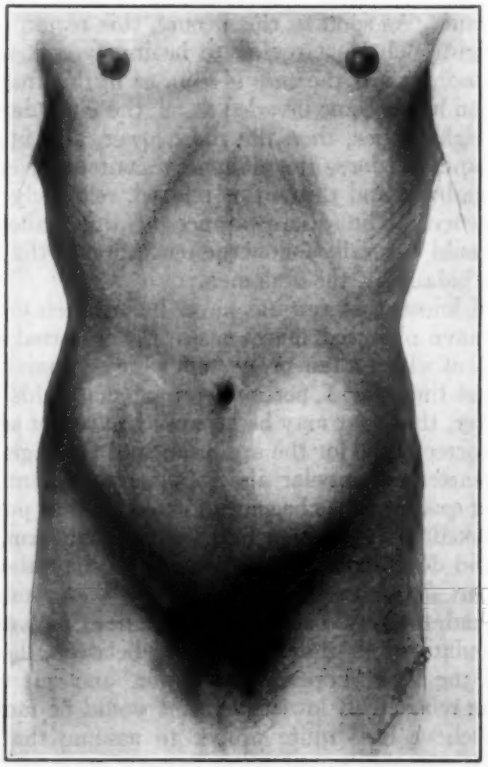

FIG. 1.—Ballooning of the left lower abdominal quadrant in the early stage of an acute duodenal perforation.

gradually subsided as the relaxation of the rigid portion of the abdominal wall increased.

The ballooning of the left lower abdominal quadrant as an early sign of perforation of a duodenal ulcer is not as incongruous nor as incompatible with the mechanism of the lesion as might at first glance be assumed. In fact, the explanation of this phenomenon is not difficult and was arrived at by logical deduction during the course of the examination, so that it was possible to make a correct

preoperative diagnosis. Perforation of an ulcer of the duodenum in the right upper quadrant produces almost immediate and intense "défense musculaire" of the upper half of the right abdominal musculature, notably the upper half of the right rectus abdominis. The seepage from the perforation is first downward toward the right iliac fossa, which is followed by the muscular spasm of the right lower quadrant, only second in degree to that of the right upper quadrant, as in this case. The spread of the extravasation and incidentally the peritoneal contamination is then toward the left upper quadrant. As soon as this occurs, this region becomes irritated and rigid. The last region to be involved is naturally the left lower quadrant. If the case is seen, as in this instance, before this last region has become invaded at all, the muscular contraction of first the right upper, then the right lower, and finally the left upper quadrant, will force the abdominal contents over toward the left lower quadrant and throw this relaxed, relatively normal area into prominence. The disappearance of this ballooning under anesthesia would naturally follow the relaxation of the rigid musculature of the balance of the abdomen.

As far as I know, this sign has never before been described, and although I have observed many cases of perforated duodenal or pyloric ulcer, of which a fair proportion were comparatively recent, this is the first time that I, personally, have made this observation. I feel, however, that that may be because I have not seen the cases at just the correct time for the appearance of this sign, with a perfect three-quarter rectangular abdominal involvement, and before the left lower quadrant has become affected, or that possibly I may have overlooked the symptom in a less marked form. The muscular tone and development of the individual may also play a rôle in bringing out the sign. It is probable that the prominence of the left lower quadrant would be more pronounced in patients with a flabby musculature, so that a contrast between the contracted rectangle of the right upper, right lower, and left upper quadrants and the relaxed left lower quadrant would be more apparent. Further, I believe it is quite proper to assume that the degree of evidence of the sign would be in inverse ratio to the amount of adiposity of the abdominal wall. On analysis one may really consider this sign as merely the exaggerated expression of that condition which I have frequently noted in acute duodenal or pyloric perforation, and which has been most helpful in making a diagnosis and localizing the lesion. Unless the case is so far advanced that general invasion of the abdominal cavity exists, or unless there has been an unusually large perforation with an actual flooding of the entire abdomen with duodenal contents, one will almost invariably find the following picture on careful abdominal palpation. The first and greatest rigidity, and incidentally sensitiveness, which runs approximately parallel with the

rigidity, will of course be found in the right upper quadrant. The next greatest is almost always in the right lower, the next in the left upper, and the last and least in the left lower quadrant (Fig. 2). Though, of course, the division of the four abdominal quadrants is not sharply defined, the definition is usually distinct enough to be recognized with comparative ease. The observation of this arrangement of the variation in the rigidity and sensitiveness in the various abdominal quadrants, sometimes very marked, but often just barely

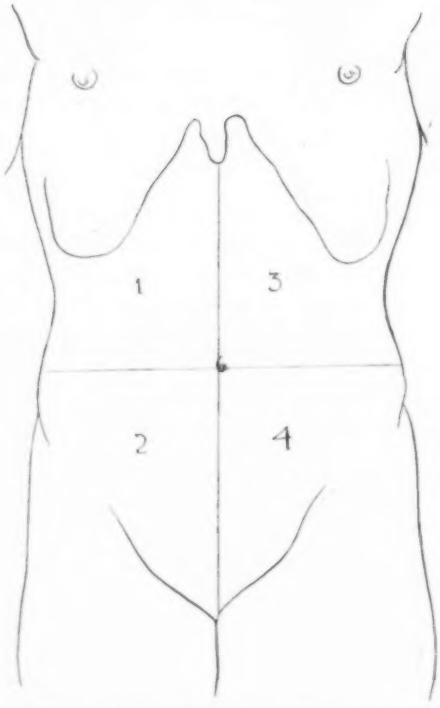

FIG. 2.—Diagram illustrating the characteristic spread and arrangement as regards both time and degree of the rigidity and sensitiveness in acute duodenal (or pyloric) perforation. 1, first and greatest; 2, second; 3, third; 4, last and least.

perceptible and detected only by the most careful and painstaking examination, has on numerous occasions helped to differentiate a perforated duodenal ulcer from an acute perforative appendicitis with spreading peritonitis, and led to the correct placing of the incision in the upper instead of in the lower abdomen. The absolute amount of the rigidity and sensitiveness may vary, depending largely upon the time factor, but unless there is a generalized peritoneal involvement their relative intensity and the direction and progress of the invasion is usually as described.

In acute perforative appendicitis with spreading peritonitis there is an analogous but contrasting picture as regards the rigidity and sensitiveness, and also with a definite, systematic and typical progression. Of course, the first and greatest rigidity and sensitiveness will be in the right lower quadrant. The next will be in the left lower, then in the right upper, and the last and least in the left upper (Fig. 3). This is the usual arrangement and is generally found in the progressive type of the disease before the peritonitis has become

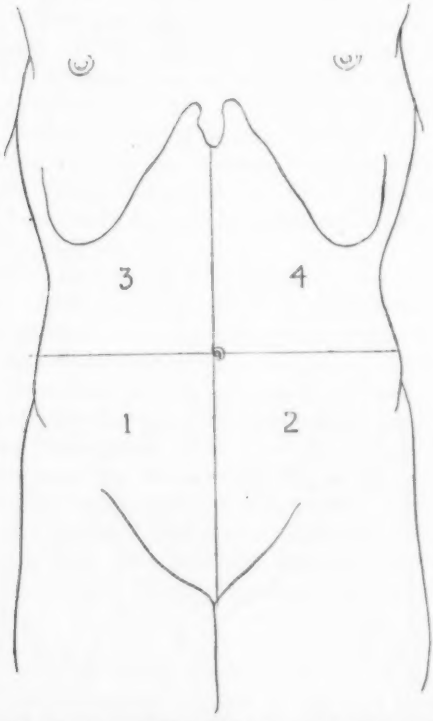

FIG. 3.—Diagram illustrating the characteristic spread and arrangement as regards both time and degree of the rigidity and sensitiveness in the usual variety of acute perforative appendicitis with progressive peritonitis. Here the appendix is generally subcecal with the tip pointing inward or downward. 1, first and greatest; 2, second; 3, third; 4, last and least.

generalized. It depends upon the most common location of the appendix in the subcecal region, with the tip pointing inward or downward toward the pelvis. If the appendix points upward retrocecally, especially if the tip lies under the right lobe of the liver, this sequence may vary so that after the right lower quadrant, the right upper quadrant may be the next in time and degree to show the rigidity and sensitiveness, then the left lower and finally, as in the normal form of spread, the left upper (Fig. 4). A balloon-

ing of the left upper quadrant analogous to that described in the left lower in acute duodenal perforation, would be unlikely in acute perforative appendicitis, mainly because of the greater fixation and the greater physiologic tenseness and retraction of this segment of the abdominal wall. Just as a diagnosis of perforated duodenal ulcer has frequently been made and differentiation from acute perforative appendicitis with progressive peritonitis established by

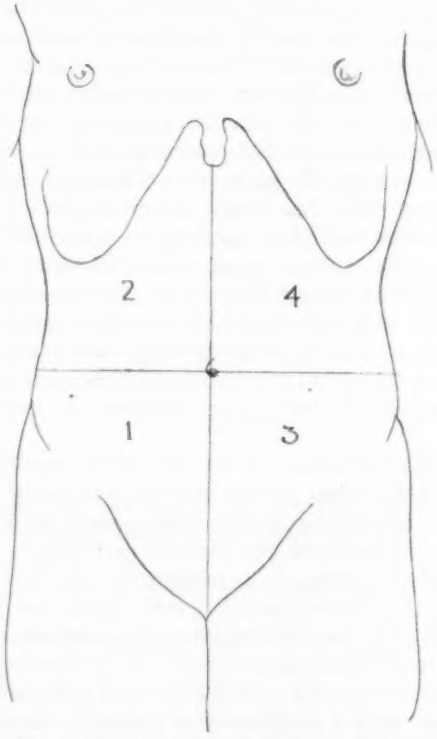

FIG. 4.—Diagram illustrating the characteristic spread and arrangement as regards both time and degree of the rigidity and sensitiveness occasionally found in acute perforative appendicitis with progressive peritonitis. Here the appendix is generally retrocecal with the tip pointing upward. 1, first and greatest; 2, second; 3, third; 4, last and least.

noting the characteristic variation in the abdominal rigidity and sensitiveness, so has the reverse been true and an acute perforative appendicitis with spreading peritonitis been recognized and differentiated from a duodenal perforation by observing the typical arrangement of these signs in the former condition.

In severe acute lesions of the left lower quadrant, such as in acute diverticulitis of the sigmoid with spreading peritonitis, the arrangement of the rigidity and sensitiveness is usually first and greatest

in the left lower, next in the right lower, then in the left upper, and finally, the last and least, in the right upper quadrant. For the same reason as referred to above when discussing acute perforative appendicitis, no ballooning of the right upper quadrant would be likely to occur.

For the sake of completeness, it should be mentioned that in serious acute lesions of the left hypochondrium with progressive peritoneal involvement, such as perforated ulcer of the fundus of the stomach, perforation of the splenic flexure of the colon, or rupture of the spleen, the logical distribution and sequence of the rigidity and sensitiveness should be first and greatest, the left upper, next the left lower, then the right upper, and finally the right lower quadrant. Owing to the relative rarity of left hypochondriac lesions, the opportunity has not presented itself to study this phase of the problem as carefully as in acute duodenal and appendicular perforations, but what has been observed tends to confirm this deduction. Further, if such a case, with an acute left hypochondriac lesion is seen at the proper stage, a ballooning of the right lower abdominal quadrant should also occur. At any rate, if the interpretation of the observation, which has been made and which is herein reported, is correct, it is certainly conceivable that a corresponding sign in the right lower quadrant is possible as an indication of an acute lesion in the left hypochondrium and should be borne in mind.

Naturally, this ballooning of the left lower quadrant, which has been noted and described in this report, could occur in other acute perforations in the right hypochondrium, such as a perforation of a pyloric ulcer, or an acute gall bladder perforation. The latter is, however, relatively unusual, a perforated duodenal is somewhat more common than a perforated pyloric ulcer, and finally, from a practical standpoint, the differentiation of a duodenal from a pyloric perforation is really quite immaterial. It is, therefore, a fairly safe assumption that if this sign is indicative of a perforation in the right hypochondrium, such a perforation is probably duodenal, the most usual type of right hypochondriac perforation. Even if an exact diagnosis cannot be made, the sign at least points to the location of the lesion in the right hypochondrium. The important point, of course, from a differential standpoint, is not to be misled by this sign into believing that one is dealing with an intestinal obstruction due to a volvulus in the left lower abdomen, for which it may readily be mistaken. To be sure, in either instance one would be faced with an acute abdominal emergency requiring immediate operation. It is nevertheless obvious that, if possible, a correct anatomical and pathological diagnosis should be made before operation so that the incision can be properly placed in the upper abdomen and the operative procedure planned in advance to avoid unnecessary delay and disturbance.

Summary. 1. A definite ballooning of the left lower abdominal quadrant has been noted in a case of perforated duodenal ulcer. It is believed that this symptom is an early sign of an acute perforative lesion in the right hypochondrium which is usually a perforation of an ulcer of the duodenum, and that it is produced by the contraction of the right upper, right lower and left upper abdominal quadrants, which have become invaded and rigid, while the left lower quadrant is still uninvolved and relaxed. It is important that the significance of this sign and the mechanism of its development be recognized to avoid making the erroneous diagnosis of a volvulus in the left lower abdomen, which it strongly suggests.

2. It is thought that this sign simply represents an early and exaggerated stage of a condition frequently noted in acute duodenal or pyloric perforation, namely, a characteristic spread and arrangement of the rigidity and sensitiveness as regards both time and degree, the first and greatest being in the right upper, the next in the right lower, the next in the left upper, and the last and least in the left lower abdominal quadrant.

3. Analogous but contrasting progression and distribution of the rigidity and sensitiveness can be observed in other acute abdominal perforations with spreading peritonitis, notably in acute perforative appendicitis with progressive peritonitis.

ATYPICAL ACUTE MYELOID LEUKEMIA WITH UNUSUAL PULMONARY MANIFESTATIONS.

Case Report with Necropsy Findings.

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Although well aware of the fact that cases of leukemia at times have bizarre clinical features, the case herewith presented had such an unusual course that we feel warranted in recording it in the literature. The long period of observation, the lethal outcome and necropsy enabled us to obtain complete clinical and pathologic data.

Case Report. On February 15, 1926, Mrs. L. R., aged thirty-eight years, Russian and married, consulted one of us (H. J.) for a productive cough of eight weeks' duration; paroxysms of coughing

were often followed by emesis. Profuse sweats had occurred. There had been no hemoptysis. A loss of 20 pounds in weight was reported at this time. The physical examination at this office visit disclosed pallor, perforation of the nasal septum and râles throughout the right chest and left apex. The mouth temperature was 100.4° F. The blood pressure was 100 mm. Hg. systolic and 50 diastolic. On March 11, radiographs of the chest and sinuses revealed, respectively, infiltration of the right hilum and of the right base, and cloudiness of the left ethmoid cells. The sputum was negative for tubercle bacilli.

On March 17, 1926, the patient was admitted to the Beth Moses Hospital for further study. Her chief complaints on admission were cough, pain in right side of chest, weakness, loss in weight (25 pounds over a period of four months), fever and night sweats. The family history and past personal history were essentially unimportant.

About four months prior to her entrance into the hospital, the patient suffered an indisposition which was diagnosed as grippe. The cough and generalized body pains necessitated her confinement to bed, where she has remained throughout practically the entire period of her illness. The persistent severe cough, productive in nature, was accompanied by right-sided chest pain, daily low-grade temperature and profuse night sweats. The increasing weakness and loss in weight were pronounced. Other symptoms noted were anorexia, vomiting, belching, constipation, palpitation and occasional headaches.

The pulmonary aspects of the case were prominent throughout the entire period of observation. Symptoms and signs referable to other organs, well worth comment if occurring alone, were almost completely overshadowed by the pulmonary phases of the case. The harrassing cough, frequently so severe as to induce vomiting, rusty or frankly sanguineous sputum, the dyspnea and occasional chest pains, at all times directed attention to the lungs. From the day of admission, when involvement of the right apex was discovered, abnormal physical signs could almost always be elicited in the chest. The migratory character of the lung lesions was especially striking. An accurate conception of this phase of the case may be had from the appended chart, wherein the roentgenographic findings and corresponding clinical signs are set forth in sequence. The reproductions of the roentgenographic films are also of service in this connection. The infiltration of the right hilum and base observed on March 11 had, at the time of admission, been succeeded by a similar process at the right apex. Dullness, fine crackling râles and bronchovesicular breathing persisted over this area for at least thirteen days. On April 3, a distinct friction rub was heard in the region of the right scapula. Four days later numerous fine pleuritic râles were found below the angle of the left scapula. On April 9, before the left apex had entirely cleared, signs

of consolidation appeared in the right lower lobe, as indicated by dullness and bronchial breathing. Evidences of complete resolution were lacking until May 10. During this period of one month, one or more physical signs, such as dullness, friction rub, distant voice sounds, egophony and râles, were always elicited at the right base. On April 29, the intense pain in the right chest was associated with elevation of temperature and expectoration of blood-tinged sputum. The involved area was punctured on two occasions, without yielding anything of diagnostic value. Before the right lower lobe had entirely resolved, evidences of infiltration (dullness, bronchovesicular breathing, subcrepitant râles) appeared, first, in the left lower lobe and five days later, in the left upper lobe. The left basal signs disappeared within a week. The process at the left apex persisted, clinically, for one month. The laryngitis which developed at this time was investigated by the laryngologist who reported marked anemia of the larynx and pharynx throughout; slight ulceration of the tip of the epiglottis on its laryngeal surface; slight ulceration and infiltration of the true vocal cords and moderate edema of both arytenoids. On June 7, the lungs were entirely clear and apparently remained so until June 22, when a distinct pleural friction rub could be detected in the posterior axillary line, about the level of the right tenth rib. A transient edema of the lungs, recurrence of physical signs at the right apex, and the terminating respiratory difficulty completed the pulmonary picture.

CHART I.

Date.	Roentgenographic report.	Clinical notes.
March 11	Infiltration of right hilum and right base.	Râles throughout right chest and left apex.
March 25	Right upper lobe pneumonitis. Thickened pleura right upper lung field. Peribronchitis (general).	Dullness and râles at right apex. Signs strongly suspicious of tuberculosis.
April 12	Entire resolution of right upper lung field.	Right apex clear clinically. April 9th, bronchial breathing at right base.
April 29	Right lower lobe pneumonia.	Lesion first discovered clinically April 9th.
May 12	Left upper lobe pneumonitis. Resolving right basal infiltration.	High pitched resonance and numerous râles over left apex, May 8th.
May 24	Infiltration left upper lung field, partly bronchopneumonic and partly parenchymatous. Right base lesion less marked.	Dullness with numerous coarse râles at left apex.
June 12	Processes at right base and left apex cleared up to great extent.	General condition better than at any time previous.
June 24	Right diffuse bronchopneumonic infiltration. Left bronchopneumonic infiltration of lesser degree.	Pleural friction rub in right posterior axillary line at level of 10th rib. Harsh breathing with few râles at left base. Diminished breathing with a few fine crackling râles at right base.

The various additional clinical manifestations noted during the course of the illness, may best be grouped as follows: The splenomegaly, first apparent one week after hospitalization, was associated with progressive enlargement of peripheral lymph nodes. Enlargement of the right supraclavicular chain of lymph nodes was followed in turn by palpable involvement of axillary, left supraclavicular, right posterior cervical and inguinal groups. The skin was the seat of a generalized hirsuties, most marked on the face and body. The pronounced pallor was early blended with a café-au-lait hue. The increasingly intense brownish pigmentation was eventually not unlike that found in subacute bacterial endocarditis. Additional skin lesions developing in the later stages of the illness were a fine petechial eruption over the wrists and left shoulder, and violaceous nodular swellings suggestive of leukemic infiltrations. The latter made their appearance, singly and in crops, over the abdomen, right mastoid region, in the axillæ, over the right and left thighs, suprascapular region, to the right of the umbilicus and at the angle of the left mandible. One of these nodules was excised for microscopic examination. Generalized pruritus was a late occurrence. Central nervous system involvement was indicated by a profound convulsive seizure and great impairment of vision with negative ophthalmoscopic findings. The convulsion and postconvulsive twitchings occurred about six and a half months after the onset of the illness and were ascribed by the neurologist to multiple capillary hemorrhages or an encephalitic process. The cardiac manifestations came late in the disease and consisted of apical systolic murmur and fetal rhythm. Slight pretibial edema was present. The tender, ballotable mass, palpated in the right upper quadrant, eventually proved to be a tender right kidney. The gastrointestinal disturbances were often prominent; the frequent emesis induced by paroxysms of coughing interfered with proper alimentation. There was one prolonged attack of diarrhea associated with vomiting after meals. Pyrexia of an irregular type was present throughout. The daily temperature fluctuated from 99° F. to 105° F., for the most part ranging from 101° F. to 102° F. Profuse sweating often occurred. Involvement of the lungs apparently had little influence on the temperature curve. The systolic blood pressure varied from 72 to 120 mm. Hg, with most of the readings below 100. The diastolic pressure varied from 44 to 84 mm. Hg., with most of the readings below 60.

The hematologic aspects contributed greatly to the interest in this case. Frequent studies were made as can be seen from the tabulated chart, mainly for purposes of establishing the identity of the blood dyscrasia. A profound anemia existed throughout, despite two transfusions of whole blood. The anemia was, for the most part, of the hyperchromic type. Of much greater significance was the pronounced leukopenia which obtained during the first

month of observation. For this period, the total leukocyte count never exceeded 5200 cells per cubic millimeter of blood, the majority of the counts being below 4000. After the first month there was a sudden increase in cells to almost 9000 per cubic millimeter, followed by a rise and depression to 8000 per cubic millimeter of blood. The total leukocyte count then rose sharply to more than 27,000, remaining above the 20,000 level until the termination of the illness, when there was a marked decline to 8800 cells per cubic millimeter of blood.

The stained blood smears, at all times, revealed a striking picture. The polymorphonuclear cell never exceeded 30 per cent, and was, on occasion, as low as 5 per cent of the total leukocyte count. The remainder of the leukocytes present consisted primarily of large mononuclear cells which, at first, bore great resemblance to the monocyte type of cell. Subsequently, there were showers of cells which were undeniably of primordial origin. Morphologically, these large cells were not unlike the typical Naegeli myeloblast; the large mononuclear cell with deeply basophilic protoplasm which shows four or five nucleoli in a lighter azure-staining nucleus. These cells gave a consistently negative oxidase reaction, the Goodpasture method being employed. It was only later, with marked increase in the total leukocyte count, that cells appeared with slight nuclear indentations suggestive of the so-called pre-myelocyte. Eosinophilic and basophilic cells were absent practically throughout the period of observation. The erythrocytes showed some poikilocytosis, anisocytosis and polychromatophilia. An occasional macrocyte and normoblast were observed.

Additional laboratory data are as follows: Of the 27 urinalyses performed in the course of the illness, the specific gravities varied from 1005 to 1024, the lower figures obtaining toward the end. Albumen, absent in the beginning, was voided in large amounts in the later stages. Traces of bile were found in the last month of observation. Formed elements, leukocytes, erythrocytes, hyaline and granular casts, were present in the urine in increasing numbers as the illness progressed. The blood chemistry analyses showed normal figures on two occasions, this absence of azotemia being noteworthy in the light of subsequent necropsy findings. The blood Wassermann test was negative on three occasions. The blood culture was sterile. Nine sputum specimens were examined for tubercle bacilli without success. Smears and cultures of sputum failed to reveal any unusual organisms such as spirochetes, actinomyces or Vincent's organisms. The chest punctates yielded nothing of note. A fractional gastric analysis disclosed nothing of importance. The result of the biopsy performed on June 18 (skin nodule excised from the right thigh) will be discussed with the pathologic aspects of the case.

CHART II.

Hematologic Chart.

Date.	R. B. C. per c.mm. blood.	Hb. per cent.	W. B. C. per c.mm. blood.	Polys per cent.	Mononuclear* cells all types, per cent.	Remarks.
3–17–26	1,520,000	55	3,400	16	84	Poikilocytosis.
3–19–26	1,488,000	55	3,200	16	84	
3–21–26	1,440,000	50	3,600	23	77	
3–23–26	....	..	....	..	..	Transfusion, 300 cc. whole blood.
3–25–26	2,314,000	55	3,200	17	83	
3–26–26	2,420,000	55	3,800	20	80	
3–28–26	2,176,000	55	5,200	16	84	
3–30–26	2,454,000	55	3,400	17	83	
4– 3–26	2,208,000	55	4,000	22	78	
4– 5–26	2,008,000	55	....	..	....	Platelets, 280,000 per c.mm. blood.
4– 7–26	1,664,000	55	4,400	20	80	
4–10–26	1,504,000	50	....	..	..	Transfusion, 500 cc. whole blood.
4–13–26	1,792,000	55	4,200	24	76	
4–18–26	1,696,000	55	5,000	30	70	Negative oxidase reaction.†
4–24–26	1,760,000	55	....	..	..	Negative oxidase reaction.†
4–29–26	2,364,000	55	8,800	22	78	
5– 4–26	2,016,000	55	10,600	19	81	
5–10–26	1,928,000	45	13,200	9	91	2 normoblasts.
5–20–26	2,016,000	45	11,400	5	95	
5–26–26	1,920,000	45	8,400	10	90	
6– 1–26	1,472,000	40	8,800	8	92	
6– 6–26	....	40	27,200	14	86	
6– 7–26	1,736,000	40	25,400	22	78	
6–10–26	....	..	....	..	..	Negative oxidase reaction.†
6–12–26	1,728,000	45	20,800	10	90	
6–23–26	1,760,000	45	21,200	11	89	
6–25–26	....	..	8,800	..	..	Negative oxidase reaction.† Anisocytosis, poikilocytosis and some polychromatophilia.

* The differential counts were done by house officers who apparently experienced difficulty in distinguishing the various types of mononuclear cells. On closer scrutiny we find the great majority of these cells to comprise the primitive type of cells discussed in the text.

† Negative oxidase reaction refers to the absence of oxidase granules in the abnormal, premature mononuclear cells.

Necropsy (twenty hours after death). The salient points of the necropsy protocol are as follows:

The body is that of a middle-aged woman, whose skin presents a pale brownish hue throughout. Purplish, nodular lesions, varying from 0.5 to 2.5 cm. in diameter, are to be seen on both thighs and abdomen. There is marked hirsuties of face, extremities and lower abdomen.

On opening the thorax numerous dense adhesions and firm fibrous bands are found between the parietal and visceral pleuræ on both sides. There are about 150 cc. of clear, amber fluid in the left pleural cavity. The pleura is universally thickened, more so over both apices and right lower lobe. There are no interlobar adhesions. The tracheobronchial lymph nodes are enlarged, succulent and cellular on cut surface. On gross section, the right lung presents prominent, grayish lesions, particularly at the apex and dependent portion of the lower lobe. These areas are firm, fairly well circumscribed and stand out above the cut surface. They are irregularly circular in outline, and 2 to 5 cm. in diameter.

The central portion of these nodules has the firm, resilient consistency of connective tissue, the periphery being less dense and more cellular in nature. The normal pulmonary markings are lost. The remainder of this lung is congested, moist, though fairly well aërated. A similar type of nodular lesion is found in the substance of the left upper lobe. The left lung is otherwise edematous and congested.

The pericardial sac contains about 200 cc. of serosanguineous fluid. Numerous smaller and larger petechial spots are visible throughout the visceral pericardium. A shaggy, fibrinous exudate is likewise present, most marked anteriorly. The left ventricle is dilated, its wall somewhat thickened. The myocardium is blanched, soft and friable. On closer gross inspection it is seen to be stippled with punctate, gray-white areas. The valves are intact. The aorta is grossly normal.

On opening the peritoneal cavity, a small amount of serous fluid is evacuated. The peritoneum is everywhere smooth, pale and glistening.

The liver is enlarged (weight, 3200 gm.). Its cut surface has a nutmeg appearance. There are, in addition, myriads of minute, miliary-like elevations, diffusely scattered throughout the organ. The gall bladder is grossly normal.

The stomach and intestines show no gross abnormalities aside from marked pallor. There are numerous bean- to walnut-sized lymph nodes in the mesentery. The retroperitoneal lymph nodes are similarly enlarged. On section these nodes are pale and succulent. The pancreas is grossly normal.

The spleen is enlarged (weight, 560 gm.). The capsule is smooth. It is soft and friable and its rather diffluent, red substance is studded with minute pale nodules. The Malpighian bodies can be made out with difficulty. One recent infarct can be seen at the upper pole.

Both kidneys are moderately enlarged (combined weight, 380 gm.) and symmetrical in appearance. The capsules strip easily; there are no surface irregularities. On cut section, marked pallor is seen. The medullary substance appears, in places, imperfectly distinguishable from the pale cortical substance. Minute grayish areas can be made out, especially in the cortex. Aside from moderate enlargement, the adrenals appear normal.

The uterus and tubes present no gross abnormalities. The ovaries are small and sclerotic. The right ovary contains a few small cysts, from which clear limpid fluid can be expressed.

The bone marrow of the sternum and lumbar vertebræ is red and congested.

Cross-section of skin nodules on the right thigh and abdomen reveals, in all, a circumscribed, grayish, homogeneous lesion in the subcorium.

Histology. Paraffin sections were made from all the formalin, alcohol and Zenker-fixed tissues. The preparations were stained with hematoxylin and eosin, iron hematoxylin and with the Giemsa method. The result of the microscopic studies of these stained slides is briefly as follows:

The center of the pulmonary nodular lesion is found to consist solely of dense avascular connective tissue, which merges into a thick peripheral rim of myeloid cells. The capillaries in the vicinity of the nodule are distended with thrombi of the same type of cell. The pleural hyperplasia is the result of an intense fibrotic process, with superimposed myeloid-cell infiltration. From microscopic studies of the lesions, one gains the impression that the pathologic picture is the result of repeated infarctions secondary to vascular occlusions with myeloid cells. Pulmonary parenchyma and overlying pleura are both involved in this infarctive process.

The pericardium shows the same type of productive lesion observed in the pleura. The heart muscle presents a remarkable degree of myeloid infiltration, unsuspected from the gross examination. The muscle fibers are so separated and split up by these cellular elements, that they appear often as isolated cells or single strands of muscle tissue. Numerous capillaries are plugged by thrombi made up of these abnormal cells. The pronounced invasive character of this disease process is, perhaps, best seen in the histological sections of the heart muscle.

The liver shows typical leukemic infiltrations, chiefly interacinar. In addition, there is the well-advanced, central liver cell atrophy of prolonged passive congestion.

The spleen has lost the normal architecture as a result of replacement by masses of myeloid cells. The Malpighian bodies are almost obliterated. The sinusoids and intervening pulp tissue are densely infiltrated with the cells in question.

The lymph nodes, tracheobronchial, retroperitoneal and mesenteric, all show evidences of myeloid substitution.

The kidneys show a marked degree of myelopoiesis. The interstitium is, in places, so closely packed with abnormal cells as to crowd out the glomerular and tubular elements. The glomeruli, where present, are intact. The tubules are undergoing marked degenerative changes; many of the nuclei are fragmented and pyknotic; the cytoplasm is universally granular and hydropic.

The adrenals show myeloid change, practically limited to the medulla.

Microscopic sections of bone marrow show marked overgrowth of myelopoietic cells, resulting in almost total exclusion of erythropoietic elements.

Intravitam and necropsy specimens of cutaneous nodules show, in each instance, dense masses of myeloid tissue in the subcorium.

The morphologic studies permit of this conclusion: that the

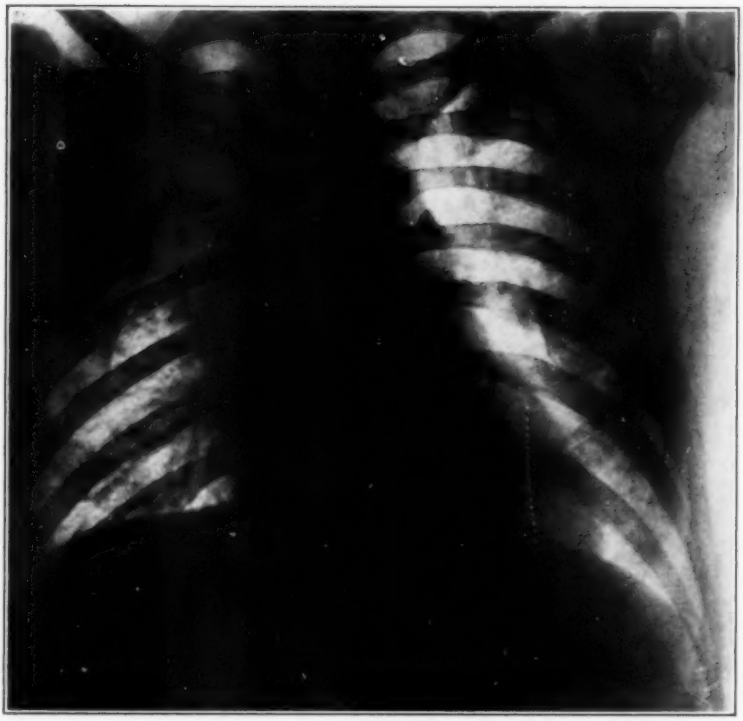

FIG. 1.—Right upper lobe pneumonitis. Thickened pleura right upper lung field. Peribronchitis. (General.)

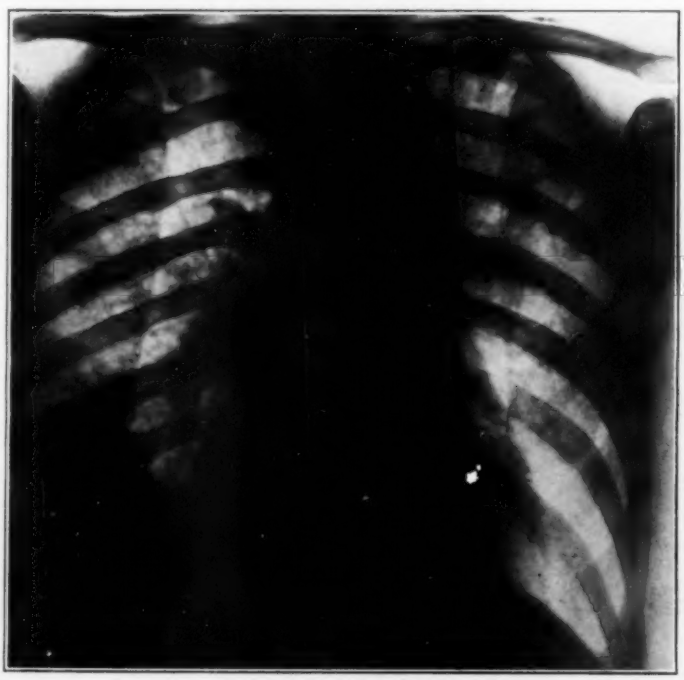

FIG. 2.—Entire resolution of right upper lung field.

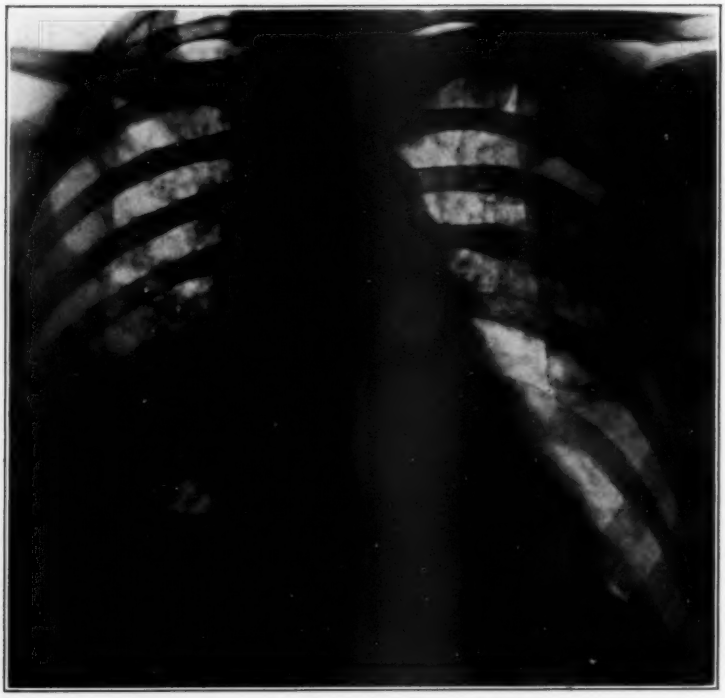

FIG. 3.—Right lower lobe pneumonia.

FIG. 4.—Left upper lobe pneumonitis; resolving right basal infiltration.

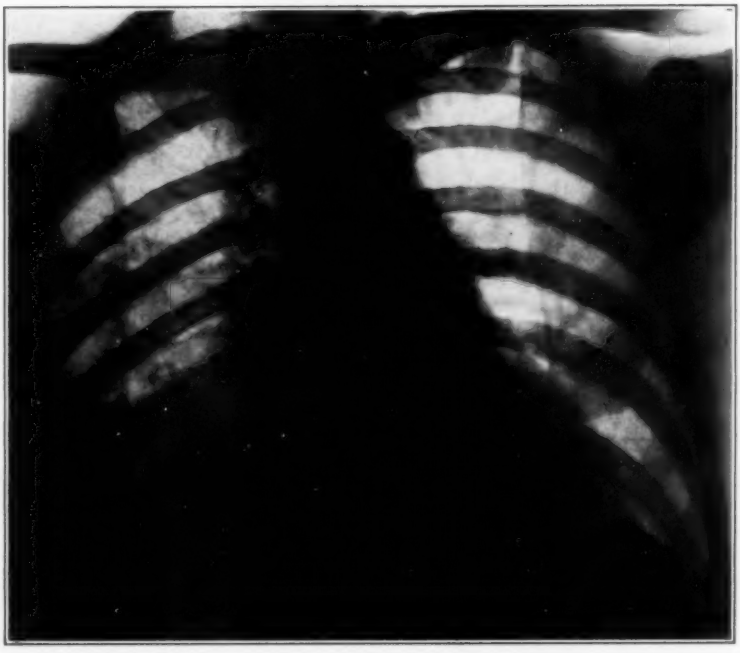

FIG. 5.—Infiltration left upper lung field partly bronchopneumonic and partly parenchymatous. Right base lesion less marked.

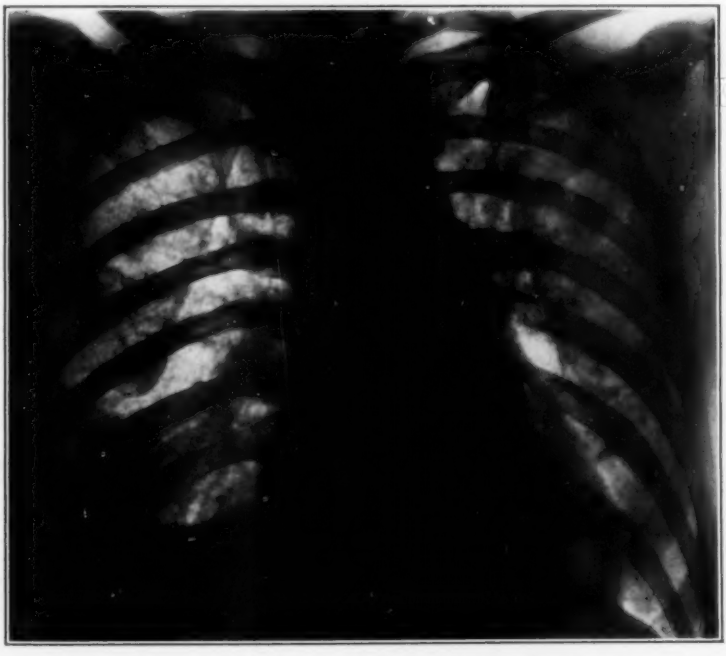

FIG. 6.—Processes at right base and left extent apex cleared up to great.

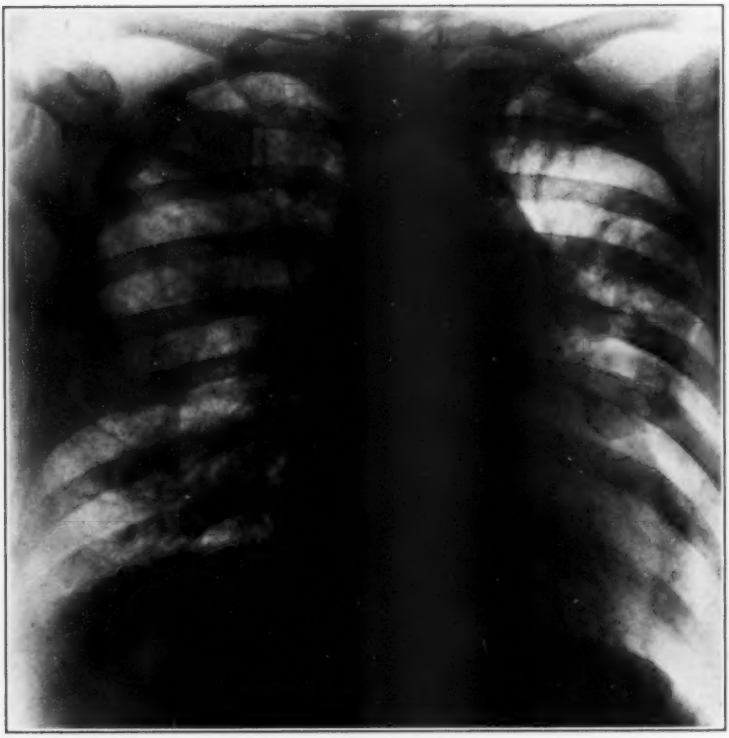

FIG. 7.—Right diffuse bronchopneumonic infiltration. Left bronchopneumonic infiltration of lesser degree.

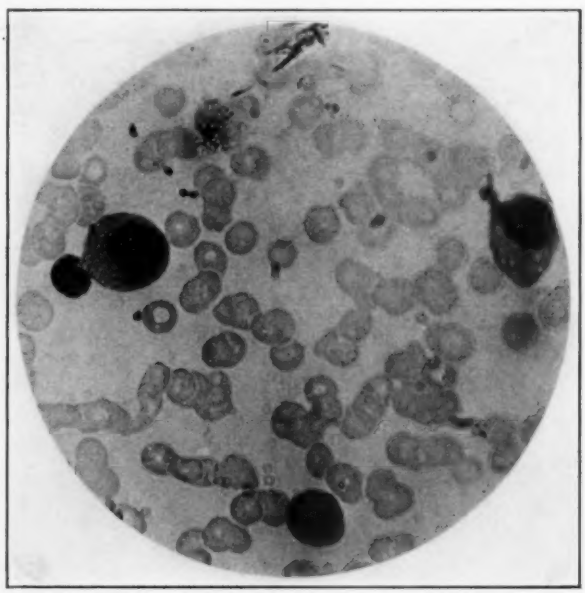

FIG. 8.—Blood smear taken in later stages of disease. Cells depicted were present in large numbers. Note beginning nuclear indentation.

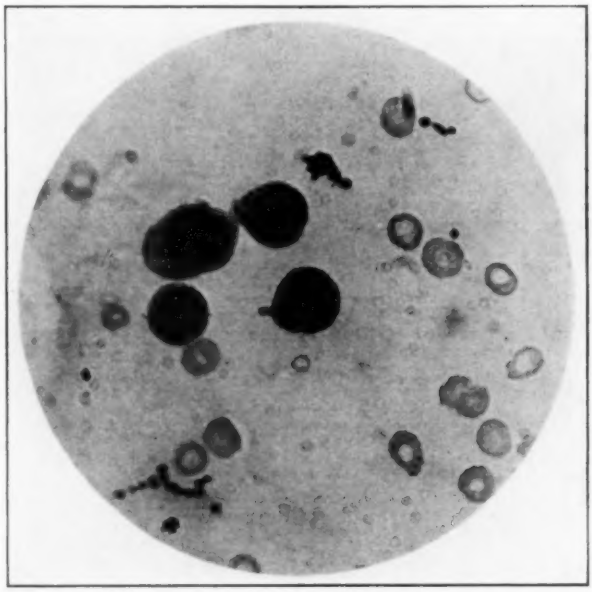

FIG. 9.—Blood smear showing more pronounced nuclear indentations of the immature cells. Note morphologic characteristics of so-called premyelocyte.

FIG. 10.—Section through lesion in right lung (upper lobe). Note dense fibrous area and rim of myeloid cells in proximity to lung parenchyma. Note also capillary myeloid thrombi.

FIG. 11.—Hyperplastic pleura with underlying lung. Note myeloid infiltration and capillary thrombi.

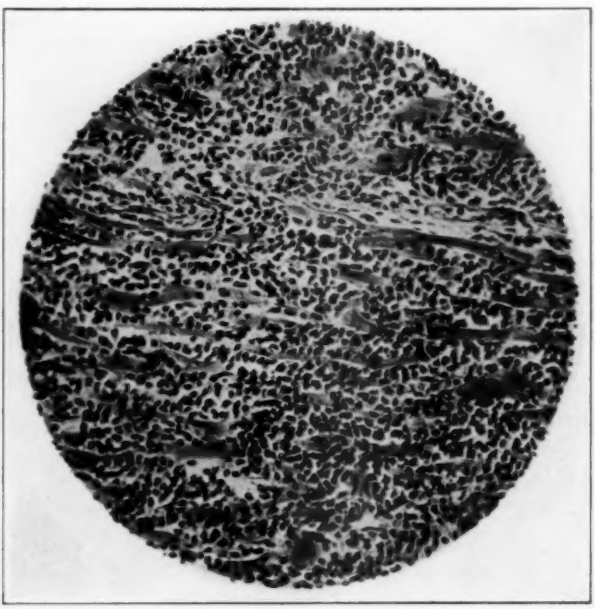

FIG. 12.—Heart muscle.—Note unusual separation of muscle fibers due to invading myeloid cells.

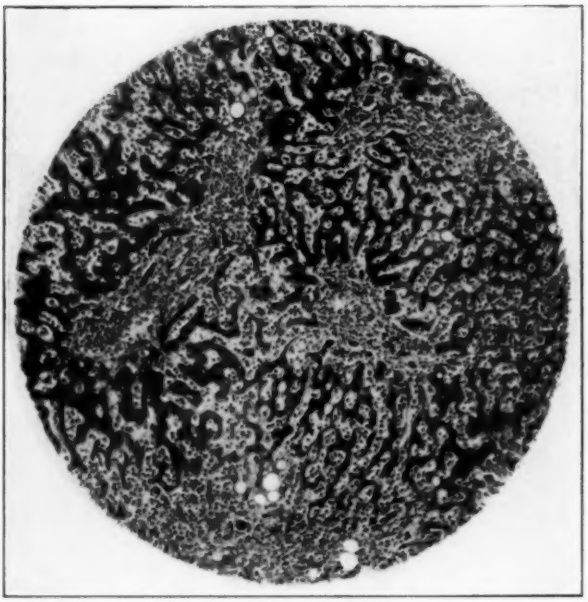

FIG. 13.—Liver. Note diffuse and focal infiltration of myeloid cells. Note also marked atrophy of liver cords.

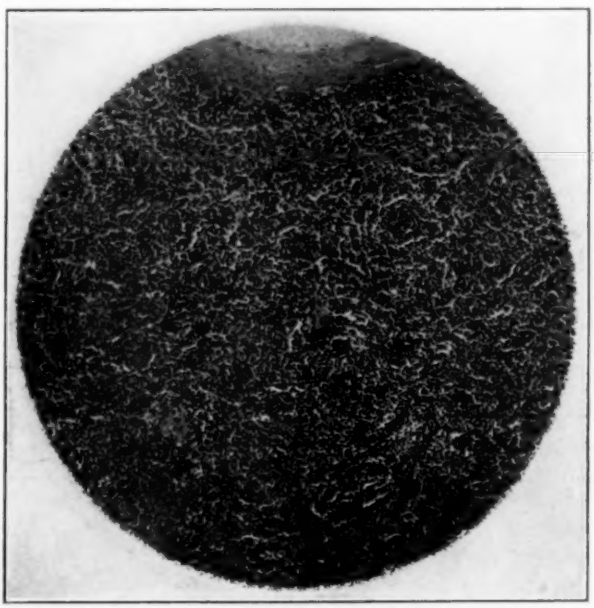

FIG. 14.—Spleen. Note intense myeloid replacement.

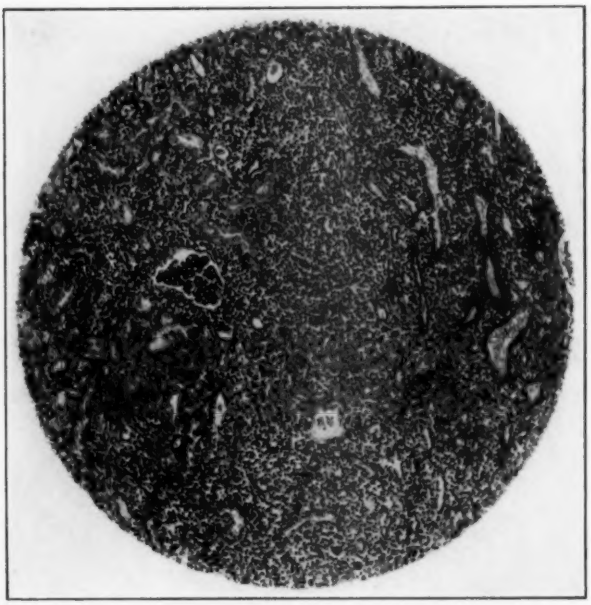

FIG. 15.—Kidney. Note intense myeloid substitution and tubular degeneration.

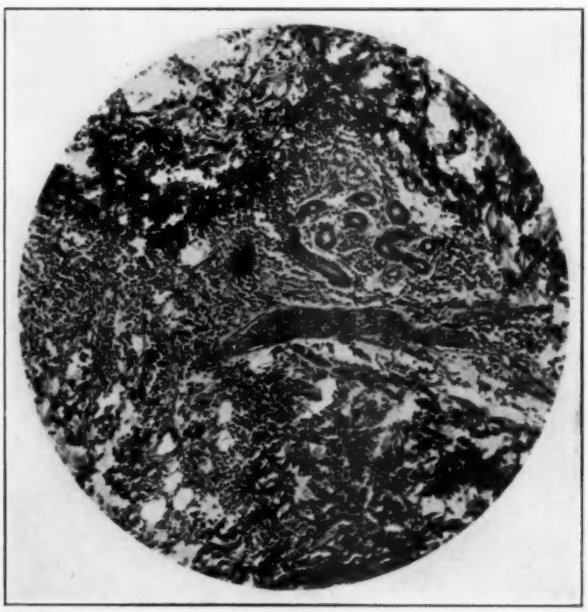

FIG. 17.—Higher power view of same. Note myeloid invasion and vascular occlusion with same type of cell.

predominant cell, and practically the only type cell, concerned in the morbid process is identical with the mononuclear cell observed in the patient's circulating blood and in the bone marrow. While probably of myeloblastic origin, it has assumed unusual invasive properties. Numerous mitotic figures can be seen in all the actively proliferating myeloid areas throughout the various organs.

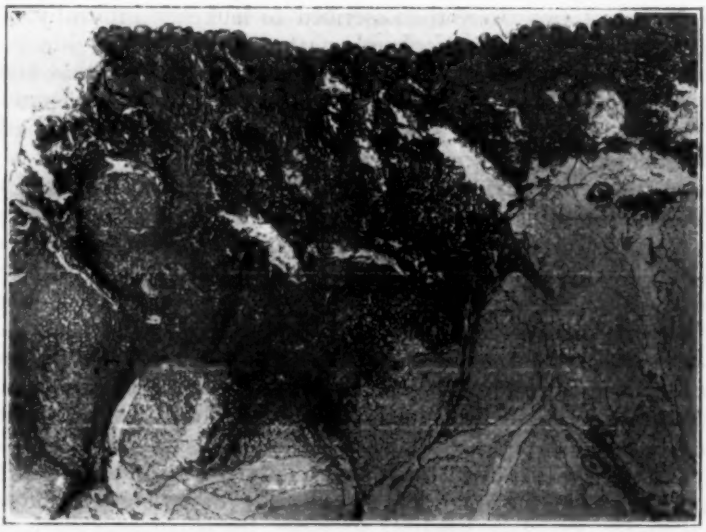

FIG. 16.—Cutaneous nodule. Low-power view for topography. Myeloid tissue mostly in subcorium.

Comment. Owing to the initial difficulty encountered in properly classifying the blood disorder, several diagnoses were entertained in an attempt to satisfactorily explain the unusual pulmonary manifestations. Pulmonary tuberculosis first suggested itself, but was soon eliminated because of the migratory and extensive character of the lung lesions, with apparent resolution. The failure to find tubercle bacilli, although looked for repeatedly, was an additional argument against this possibility. The nature of the lung lesions, the frequent recurrences and the associated symptoms were characteristic of a multiple infarctive process. The belief that a subacute bacterial endocarditis, with involvement of tricuspid or pulmonary orifices, might account for the multiple infarctions proved to be untenable. Pulmonary lues was at one time seriously considered. The perforated nasal septum and laryngeal ulceration seemed to point in this direction. A therapeutic test was made, in spite of the negative serologic findings, without favorable influence on the local or general condition of the patient. Pulmonary spirochetosis, actinomycosis, aspergillosis and a Vincent's infection

were excluded by intensive sputum studies. Hodgkin's granuloma, lymphosarcoma, leukosarcoma of Sternberg, leukemia or a leukemoid process remained as diagnostic possibilities. As the hematologic studies progressed, the leukemic nature of the disease was established. The appearance of typical violaceous nodules of leukemia cutis was additional confirmatory evidence, supported by the microscopic examination of the biopsy specimen. The pulmonary manifestations were then ascribed to leukemic infiltrations or multiple infarctions of a leukemic nature.

With complete histopathologic data at hand, we feel that many of the symptoms and signs were secondary to myeloid infiltrations of various organs. The splenomegaly and peripheral adenopathy were definitely due to myeloid replacement. The pigmentation of the skin, diarrhea, hypotension and asthenia were probably the result of adrenal infiltration. The enlarged tender right kidney and the myocardial weakness were the result of a similar pathologic process in the kidney and heart. The convulsive seizures and transient blindness of central origin were presumably the effects of an identical lesion in the cerebral cortex.

The study of the pathologic material shows clearly the predominating hyperplasia of the myeloid type of cell. The aggressive tendency of the myeloid deposits in the various organs gave rise to all grades of proliferation, from simple hyperplasia to massive tumor nodules. In fact, the invasive nature of the morbid process reminds one of the condition described by Sternberg as leukosarcomatosis. On closer analysis, however, the case under discussion bears little resemblance clinically or pathologically to this disease entity. The absence of anterior mediastinal (thymic) tumor, the remission of the pulmonary lesions which were undoubtedly of myeloid infarctive nature and the bone marrow studies would all tend to favor a myeloid type of leukemia. The only feature of the case tending to negative the latter diagnosis is the repeated failure to demonstrate oxidase granules in the offending cells. It is well known, however, that the more immature a myeloblast is, the less tendency does it have to contain oxidase granules. The presence of large numbers of undifferentiated cells and the absence of eosinophils and basophils were at first confusing. Later, the more critical morphologic studies, the tinctorial reactions of the cells and the appearance of premyelocytes made possible the diagnosis of myeloid leukemia. It might be well to mention that cases of acute leukemia are at times encountered where few or none of the transition stage premyelocytes are present. In these cases, the abnormal cells are large, resembling monocytes, and in these the oxidase test is generally negative. With rapid myelopoiesis the abnormal cell, although derived from bone marrow, may be so primordial as not to yield a positive oxidase test. It would appear, from our hematologic and histopathologic studies, that we are here dealing with a condi-

tion of this type; a case of myeloid leukemia with an atypical blood picture resulting from rapid myelopoiesis.

Of greater interest than the hematologic aspects, is the predominant pulmonary phase of the case. The pathogenesis of these ephemeral lung lesions may be traced to occlusion of pulmonary vessels by thrombi of myeloid cells with a resulting infarctive process. Resolution was apparently so complete that clinical and roentgenographic examinations failed to detect any abnormalities in the previously involved areas. A case similar to the one herein depicted has, to our knowledge, not been heretofore reported in the literature.

Summary and Conclusions. The case herein presented is unique for several reasons, as follows:

1. An initial difficulty in classifying the blood disorder was due to the absence of oxidase granules in the primordial cells, which were present in large numbers in the circulating blood. With the appearance of premyelocytes, the leukemic nature of the blood picture was evident. Thorough hematologic and histopathologic studies warrant the opinion that the case is one of myeloblastic leukemia with an atypical blood picture resulting from rapid myelopoiesis.

2. The migratory pulmonary lesions, which dominated the clinical picture throughout the period of observation, were probably of embolic, infarctive nature. This impression was confirmed at necropsy. The apparent complete resolution of these lesions was demonstrated clinically and radiographically.

3. The necropsy findings revealed a striking myelopoietic change throughout, particularly in the lungs, heart, liver, kidneys and skin.

THE CAUSE AND PREVENTION OF THE INCREASINGLY HIGH MORTALITY IN THE ACUTE SURGICAL ABDOMEN.*

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PHILADELPHIA.

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Mortality from appendicitis is increasing. Foreign as well as national statistics substantiate this fact. In England and Wales the increase during the years 1913 to 1923 was 7.3 per cent (total registration over 40 millions). In 1913 in the United States (total registration over 87 millions) the death rate was 12.1 per hundred thousand; in 1923, 14.8 per hundred thousand, an increase of 22.3 per cent. In Philadelphia there was an increase of 18 per cent between the years 1915 and 1923 inclusive. At the Samaritan Hospital there has been an increase of 16 per cent over the same period of time.

* Read before the College of Physicians, January 5, 1927.

The increase in the death rate from appendicitis is 9 per cent greater than that from cancer during the past ten years; and while the total death rate from cancer is six times that of appendicitis, four times as many people die from appendicitis before the age of fifty, which is the productive period, than from cancer.

If one were to ask the average physician today if the operation for appendicitis is a serious one, he would tell you that the mortality is practically *nil*. While this is true of subacute and chronic cases, it is surprising to know that in the average hospital in the United States one out of every 12 patients who enter the hospital with a diagnosis of acute appendicitis, dies. The mortality varies from year to year. Some years it may be as low as 3 per cent; in others it will exceed 8 per cent.

Opinions differ as to the cause of this increase in mortality. There are surgeons who believe that surgical technique and management of the patient after admission to the hospital are at fault. In England, Cecil Rowntree[1] states "that the Registrar-General's figures, which showed an increase in mortality, were accounted for by the number of inexperienced surgeons now operating and by their persistence in removing the appendix in cases where it should be more safely left." In the United States, Willis,[2] thinks that it is due to lack of standardization of methods of treatment and suggests that a commission composed of leading surgical teachers of the country be appointed to direct a thorough investigation. While it is realized by all surgeons that early operation is the ideal for which we strive, few have suggested a remedy. In Canada, however, Eberts and McKinn[3] write that the "remedy lies through the joint action of the members of such a body as the Canadian Medical Association."

I hope to show in this review of 1010 cases of the acute surgical abdomen that the cause of the high mortality rate, for the most part, is due to loss of time between the onset of symptoms and operation and that the prevention is the education of the public through the family physician. I have included six acute lesions of the abdomen which are decidedly surgical. In the order of their importance they are appendicitis, intestinal obstruction, acute perforation of the duodenum or stomach, acute pancreatitis, ectopic pregnancy, and acute perforation of the gall bladder.

Ectopic Pregnancy. In no acute surgical lesion involving the contents of the abdomen is the mortality as low as in ectopic pregnancy. Nature's provision for the perpetuation of the species is here superbly demonstrated. In no other part of one's anatomy can one lose so much blood, be operated upon and live. Postmortem examinations on patients operated upon for gall bladder disease revealed that blood not exceeding 500 cc. in amount escaped from the cystic artery and was apparently the cause of death; yet the same amount of blood of ovarian or tubal origin has been observed in the peritoneal

cavity of a young woman with few symptoms and signs to denote its presence. The time between onset of symptoms and operation has a bearing on the mortality in ectopic pregnancy; there have been but two deaths in this series of 63 cases—no mortality in those entering the hospital within twenty-four hours—a mortality of 3 per cent in those entering after that period of time.

Perforation of the Gall Bladder and Acute Pancreatitis. Perforation of the gall bladder and acute pancreatitis will be considered together. Etiologically they are directly dependent upon pathologic changes in the gall bladder which in most instances have been present for a long period of time. Acute perforation of the gall bladder with associated generalized peritonitis is most unusual. In a review of 914 charts of patients operated upon at the Samaritan Hospital for gall bladder disease, I found that 10 had perforated. Of this number, 2 had perforated into the general peritoneal cavity; 1 of these died. There was no mortality in the subacute cases. Less than a quarter of 1 per cent of patients required emergency surgical treatment. However, 2 per cent of all gall bladders operated upon had an associated acute pancreatitis. Combining the cases of gall bladder perforation with acute pancreatitis, both requiring prompt surgical intervention, we have a total of 27, less than 3 per cent of all gall bladders operated upon. While this percentage is small and relatively insignificant when compared with the first 3 acute lesions mentioned, it must be reckoned with. We can, however, deal with them in comparative safety since in this series the patients enter the hospital within an average of thirty-four hours for perforated gall bladder and thirty-six hours for acute pancreatitis. Medical measures (large doses of morphin, external applications, and so forth) having had no effect, the patient's insistence on relief from pain resulted in early hospitalization and surgical treatment. While the foregoing statement is a reflection on our treatment of these cases, its truth is borne out by the facts I will present to you regarding the management of acute appendicitis, intestinal obstruction and perforation of the stomach and duodenum.

Acute Perforation of the Stomach and Duodenum. There is no pain comparable to the pain of perforation of the duodenum with the possible exception of acute pancreatitis. The patient frequently rolls on the floor or writhes in bed, in agony. In most of these cases there is a state of severe shock because of the proximity of the lesion to the solar plexus. Moynihan reports a case where the shock accompanying the perforation was so severe that death was instantaneous. In these cases, morphin, the panacea, the smoke screen behind which hovers the destroyer Death, unless given in large doses, has no effect and the patient reaches the hospital early. In this series, 1 patient was operated upon two and one-half hours after perforation; the average for the 52 being 32.3 hours, for the recoveries 23.5 hours, and the deaths 56.1 hours. The early symp-

toms of acute appendicitis and intestinal obstruction are usually more subtle than those of perforation of the stomach, duodenum or gall bladder or of an acute pancreatitis.

Acute Appendicitis. In this series of 750 cases of acute appendicitis 338, or 45 per cent, perforated before entering the hospital. Of these, 163, or 48 per cent of all perforations and 21.7 per cent of all patients operated upon, had perforated into the general peritoneal cavity. While in the greater percentage of instances, a diagnosis of appendicitis was made by the attending physician, less than 1 per cent entered with a diagnosis of perforation. The gravity of this observation can be appreciated when we realize that 43, or 73 per cent of the 60 deaths, had perforated.

You will observe that in the recoveries the average time between onset of symptoms and operation is 69.1 hours. The average time between onset of symptoms and operation in the perforated cases was 107.3 hours. The time element is the all important factor. Comparing our minimum mortality which is 1.53 per cent in 1923 with our maximum 9.6 per cent in 1922, we find there is an increase of 72 per cent in the time which elapsed between the onset of the symptoms and operation in 1922; in 1922 there were 100 per cent more perforations and while this has a bearing on the increase in mortality, it is not so constant a factor as the time element; for example, in 1925 with a mortality of 8.82 per cent, a 476 per cent increase over 1923, we have the same percentage of perforations as in 1923 but an increase of 47.4 per cent in the time between the onset of symptoms and operation.

It is the opinion of many that pathologic changes occur in appendices with little or no pain; certainly this is not true of a perforation into the general peritoneal cavity and while the pain of a perforated appendix is not as severe as that of a perforated duodenal ulcer or an acute pancreatitis, it is so severe that these patients invariably seek medical aid immediately. One out of every 5 patients perforates into the general peritoneal cavity and is beyond the aid of anything other than operation, when first seen by the attending physician. This group is responsible for 73 per cent of our mortality. The defensive mechanism within the peritoneal cavity takes care of 52 per cent of perforations which accounts partly for the delay in the patient's entering the hospital and in part for the management by some physicians. Fortunately, the number of medical men who persist in treating abdominal pain as though it in itself were a distinct entity rather than a warning of impending danger is gradually diminishing.

Intestinal Obstruction. We have combined hernial and internal obstruction of the intestine. As would be expected, the average time between the onset of symptoms and operation is much less for hernial than for internal obstruction; 37 hours for hernial and 76.6 hours for internal obstruction, the latter being 177 per cent greater

than in hernias. Combining both types of intestinal obstruction, gives us a total of 130 cases. Of these the deaths show 120 per cent increase over the recoveries in hours from onset of symptoms to operation.

We can divide the definitely acute surgical abdominal lesions into two groups. In the first group are ectopic pregnancy, perforated gall bladder, perforated stomach and duodenum, and acute pancreatitis. Nature will, in the majority of instances, take care of the bleeding from a ruptured ectopic pregnancy. An individual suffering with a perforated gall bladder, duodenum or stomach, or acute pancreatitis will demand relief unless his symptoms are masked with morphin. The second group, acute appendicitis and intestinal obstruction warrants our serious consideration. (1) because of the insidiousness of the onset; (2) because of the patient's delay in calling a physician; (3) because of the frequency with which laxatives have been administered; (4) because of the delay due to the physician's temporizing with the patient and the patient's family.

I am in thorough accord with Dr. Cope who says "The general rule can be laid down that the majority of severe abdominal pains which ensue in patients who have been previously well, and which last as long as six hours, are caused by conditions needing surgical intervention."

It is within the domain of the family physician to teach the public but before he can teach he must take a definite stand; he should not institute medical measures and he should refuse to assume the responsibility for the patient's life in the presence of persistent acute abdominal pain. If he is broad-minded enough to suggest to his patient that a surgeon share this responsibility, the mortality in the acute abdominal lesions will be diminished.

Ectopic Pregnancy, 65 Cases.

	Cases.	Deaths.	Mortality.
Under 24 hours	18	0	0.0 per cent
Over 24 hours	47	2	4.1 per cent

Acute Pancreatitis, 13 Cases.

Average time, onset symptoms and operation; recovery	27.7 hours
Average time, onset symptoms and operation; deaths	63.0 hours

	Cases.	Deaths.	Mortality.
Under 24 hours	10	0	0 per cent
Over 24 hours	3	2	66⅔ per cent

Acute Perforation Gall Bladder.

Total number pathologic gall bladders operated upon	914
Total number perforations, local peritonitis	8
Total number perforations, general peritonitis	2
Total number deaths, perforation	1

PERFORATED DUODENAL ULCER, 52 CASES.

Average time, onset symptoms and operation; recovered . 23.5 hours
Average time, onset symptoms and operation; deaths . . 56.1 hours

	Cases.	Deaths.	Mortality.
Under 12 hours	23	1	4.35 per cent
Under 18 hours	29	2	6.9 per cent
Under 24 hours	35	4	11.4 per cent
Under 48 hours	45	9	20.0 per cent
Under 72 hours	47	11	23.4 per cent
Over 72 hours	5	3	60.0 per cent

INTESTINAL OBSTRUCTION, 129 CASES.

Average time, onset symptoms and operations; recovered . 36.1 hours
Average time, onset symptoms and operations, deaths . . 83.7 hours

	Cases.	Deaths.	Mortality.
Under 12 hours	23	3	13.0 per cent
Under 24 hours	56	5	8.9 per cent
Under 36 hours	66	9	13.6 per cent
Under 48 hours	84	22	26.1 per cent
Under 72 hours	102	31	30.4 per cent
Over 72 hours	27	17	63.0 per cent

ACUTE APPENDICITIS, 751 CASES.

Average time, onset symptoms and operations; recovered . 69.1 hours
Average time, onset symptoms and operations; deaths . . 151.0 hours

	Cases.	Deaths.	Mortality.
Under 12 hours	49	2	4.0 per cent
Under 24 hours	225	3	1.3 per cent
Under 36 hours	308	5	1.6 per cent
Under 48 hours	438	13	3.0 per cent
Under 72 hours	560	30	5.32 per cent
Over 72 hours	191	30	15.7 per cent

The following table shows the relationship which exists between the mortality and time between onset of symptoms and operation in patients entering the hospital with a diffuse peritonitis, which group is responsible for 73 per cent of our mortality.

	Mortality.	Time onset, symptoms and operations; general peritonitis.
1912–14	4.0 per cent	71.0 hours
1916–20	6.35 per cent	82.0 hours
1921	0.0 per cent	36.0 hours
1922	9.6 per cent	85.2 hours
1923	1.53 per cent	49.5 hours
1924	1.7 per cent	54.5 hours
1925	8.82 per cent	73.0 hours
1926	5.3 per cent	60.5 hours

The prevention of this increasingly high mortality lies in the reduction of the time between onset of symptoms and operation. This can be successfully brought about by obtaining the coöperation of the staff and physicians who refer patients to the hospital. We have done this at the Samaritan Hospital by sending a letter emphasizing the following points:

1. The importance of diminishing the time between onset of symptoms and operation.

2. Public education through the family physician relative to the use of laxatives in the presence of abdominal pain.

3. Time element affects the prognosis but has no bearing on the character of the pathology. Gangrene may occur as early as five hours and perforation as early as twelve.

A follow-up letter will be sent out every three months reporting progress.

	Before letter.		After letter.	
	Recovered.	Deaths.	Recovered.	Deaths.
Intestinal obstruction .	38.0 hours	83.7 hours	35.0 hours	0.0 hours
Ectopic pregnancy . .	24.0 hours	47.0 hours	24.0 hours	0.0 hours
Perforated duodenum ulcer	23.5 hours	56.1 hours	10.0 hours	0.0 hours
Appendix	65.9 hours	151.0 hours	42.6 hours	40.6 hours

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OBSERVATIONS ON THE REACTION OF NORMAL NASAL MUCOUS MEMBRANE.*

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It is important that the rhinologist be familiar with reactions of the normal nasal mucous membrane to the various environmental conditions so that he may be better able to evaluate symptoms of which a patient may complain. Many persons in robust health complain of symptoms referable to the upper respiratory tract which on final analysis may be explained on a physiologic basis. The present study was undertaken to determine the nature and extent of reactions of normal nasal mucous membrane.

From time immemorial, the popular conception of the function of the nose has been that of olfaction. This view was accepted by medical men until comparatively recent time. The ancients believed that respiration was for the purpose of cooling the blood. Helvetius, in 1729, supported this view and added that the area of the pulmonary vein was larger than that of the pulmonary artery. In 1823, Hempel asserted that the air was heated in the lungs,

* Thesis submitted to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of Master of Science in Otolaryngology, August, 1926.

Submitted for publication February 16, 1927.

making no reference to the nose or mouth as bearing part in the function, as he regarded the nose as an organ to test the quality of inspired air before it passed to the lungs. In 1829, Magendie first referred to the nose as part of the respiratory tract which helped to warm and moisten the inspired air. Adelon, in the same year, making no mention of the functions of the nose in respiration, speaks of the moisture of the expired air having its sole source in the lungs. In 1845, Vierordt asserted that the inspired air was raised to body temperature in the nose independent of the other portions of the respiratory tract.

In 1864, Grehant investigated the subject experimentally. His apparatus consisted of a glass tube containing a thermometer which was held in the mouth to permit inspired air to pass through the tube. Although his results were erroneous he recognized the importance of the nose as an organ of respiration. Even as late as 1878, Remy alluded to the nose as an organ of olfaction and stated that its other functions are purely secondary and adventitious.

At present most medical men regard the nose as essentially a respiratory organ, although in the minds of a few the olfactory function still maintains preëminence. Foster considers it just as essential for the air to be prepared by the nose before it enters the lungs as for the food to be prepared by the mouth before it enters the stomach. Bosworth says, "Every breath of air that passes through the nasal chambers must become charged with moisture." He believes that otherwise it would rapidly exert a deleterious influence on the mucous membrane of the air passages beyond by robbing them of too much moisture. The mucous membrane of the air passages beyond the nose does not possess a special apparatus for this moistening process. It contains only mucous glands which secrete mucus. Mucus is composed of 93 per cent water and 7 per cent solid matter. Robbed of a large portion of this water it becomes thick, inspissated, and annoying, thereby producing symptoms.

In the nasal mucous membrane, however, there is an apparatus capable of furnishing water, namely, the erectile tissue of the turbinate bodies. Such an apparatus is absolutely essential for the integrity of the air passages beyond. Especially is this true in a variable climate like that of Minnesota in which great changes in humidity occur.

Closely associated with the moistening process is the heating of the inspired air. The nose accomplishes this by means of the large and numerous bloodvessels and spaces under the mucous membrane. Without proper thermal change and proper moistening, serious damage of the air passages lower down would result.

Of equally definite but lesser importance is the function of the nose as a filter. This is frequently evident on inspection of the nose. Ballinger believes the vibrissæ guarding the atrium of the nostrils

act as a coarse filter by picking up grosser particles, thus preventing injurious contact with the more delicate nasal mucous membrane. Coakley maintained that most of the particles of dust and bacteria which escape the vibrissæ are entrapped by the mucus covering the surface of the nasal mucous membrane. The turbinates break up the column of inspired air causing eddies so that most of the air comes in contact with some part of the mucous membrane. This facilitates the deposit of foreign particles on the membrane. Wright and Smith assert that thin sheets of air in passing, deposit at least three-fourths of their bacterial content on the mucous surface of the nose. The dust and bacteria thus deposited in the nasal cavities are carried to the pharynx by the flow of secretion. The cilia which aid this flow anteroposteriorly are wholly immersed in the secretions which cover the surfaces. Paget believed the most important function of the nose is to filter the inspired air.

In 1884, Zuckerkandl in his classic work on the anatomy of the nose, brought out the fact that the mucous membrane covering the turbinates is a rather complex structure. It consists of connective tissue, the upper surface of which is covered with epithelium and the deep layer forms the periosteum of the turbinate bones. Between these two layers there is abundant lymphoid tissue within which are the venous plexuses which he names "swell bodies." "The definite localization of the venous plexuses differentiates it from true erectile tissue."

In 1895, Wright[33] did much original work on the vascular mechanism of the nasal mucous membrane. He believed that the larger arteries are well supplied with muscular coats. These lie in the deepest layer of the mucous membrane close to the bone and give off branches to a network of capillaries which supply the periosteum, the glands and the epithelial layer of the mucous membrane. These capillaries are collected into veins which dilate into venous sinuses, the large lacunæ of which are the deeper, and the more superficial of which are called "cortical network." These lacunæ in turn empty into the veins which accompany the primary arterioles into the periosteal layer. There is a thick network of capillaries around the ducts of the glands which will be referred to later.

Zuckerkandl believed the "swell" bodies were distributed over the lower turbinates, along the border of the middle turbinates, and at the posterior end of each. Ballinger emphasizes the localization of the erectile tissue along the free border of the inferior turbinate bodies. Wright and Smith include in their distribution the posterior border of the septum.

In 1910, Wright[32] also brought out the localization of the connective tissue of the mucous membrane. He believed the elastic fibers are found mostly in the walls of the large bloodvessels, next to the periosteum, and deeper layers of the stroma intimately associated with it. Everywhere through the middle layers of

stroma, elastic threads run parallel or obliquely to the surface. In the subepithelial layer fibers are specially arranged, as they run only vertically to the surface. There is a network of elastic tissue surrounding the glands which is of greater thickness between the epithelium and glands. The intima of the venous sinuses is very thick and the longitudinal fibers stand out with Weigert's stain. The arterioles have, proportionately to their size, more of the muscular layer than in regions of the body without erectile tissue.

Mention should also be made of glands in the nose. The prevailing type of glands in the olfactory region are tubular (so-called Bowman's glands) and secrete a watery substance. The glands of the respiratory region are the racemose type with mucous secretion.

There has been much speculation,[37] but no consensus of opinion regarding the function of the inferior turbinate bone. Ziem has noted that bloodhounds have a very large surface expansion and cleavage of the inferior turbinates rich in bloodvessels and therefore the air is well warmed. This was thought to be true of rapid-running animals; however, these folds and rollings are completely lacking in the hare and horse. Others thought that these folds and rollings were associated with a high degree of olfaction, yet the pig with acute smell has none.

Apparently little attention has been directed to the effects of the atmosphere on the mucous membrane. In 1908, Spratt pointed out that stenosis and excessive secretion are most common in cold weather, due to the extra work thrown on the nose in warming and moistening the cold dry air, Kayser noted that when cold air is inspired through the nose the blood supply in the turbinate bodies is notably increased and therefore their heating capacity is increased. Ballinger in his text says that if the air is dry the swell bodies enlarge and are just active enough to saturate the inspired air, whereas if the atmosphere is humid, they are less active.

In 1888, MacDonald, by means of a tracheal cannula attached to the nose and mouth, measured the warming function of the nose with the following interesting results: Temperature of external air at—7°, raised to 28.8° C.; at 1.7°, raised to 35° C.; at 7°, raised to 34° C.; at 12°, raised to 35.6° C.; at 45°, lowered to 33.6° C.

He found that robust persons raise the temperature 2° or 3° higher than anemic ones. Independent work by Aschenbrandt, Kayser, and Bloch at about the same time led to similar results except that their figures were 3° to 6° lower than those of MacDonald. That the humidity of the air in passing through the nose was raised to the saturation point is supported by the works of Kayser, Aschenbrandt and MacDonald. Bloch, on the other hand, concluded that the air was only two-thirds saturated.

MacDonald discovered that the quantity of aqueous vapor absorbed varied with the barometric pressure in the nose. Any

experimentally produced stenosis causing more difficult respiration increases the amount of water, and *vice versa*. It does not appear that these tests were made under varying conditions of temperature and humidity, although it is readily understood that these two factors in their mutual relations are very important.

In 1896, Goodale reported the results of considerable experimentation on the heating and moistening power of the nasal mucous membrane. He used an apparatus constructed on the principle of the aspiration psychrometer and took every precaution to avoid technical errors. The work was done under different atmospheric conditions with special reference to temperature and relative humidity. He concluded that the amount of heat and moisture imparted to the inspired air by the nasal mucous membrane is approximately proportional to the differences existing between the state of the atmosphere and that of the air in the middle air passages. He found that, with an atmospheric temperature from 1° to 5° C., air in the nose is raised to 28° C., with an external temperature from 21° to 25° C., it is raised to 31.5° or 32.5° C. With an atmospheric absolute humidity of 1.4 gm. vapor at 1°, the nose evaporates 25.6 gm. water for each cubic meter of air. From Goodale's general results it appeared that air taken in through the nose and exhaled from the mouth showed the greatest increase of temperature and relative humidity, and that air inspired and expired through the mouth showed the least increase, whereas air coming in through the nose and leaving by the same route showed an increase of temperature and relative humidity, less than in the first instance, but greater than in the second.

This apparent discrepancy was accounted for by the fact that the expired air is cooled in the nose from 34° to 29.5° C., therefore, 4.5° and some water of condensation is lost by nasal expiration. Hence, he concluded that the water running from the nose common to many persons in cold weather is due to an excess of expiratory condensation over inspiratory vaporization, rather than to increased serous transudation from the nasal mucous membrane.

Goodale's work brought out another interesting fact, that warm moist air would apparently require less evaporation than cold moist air, if the intranasal temperatures were the same in both cases, but because of the greater intranasal temperature during the inspiration of warm air, the capacity of the inspired current for moisture is so enhanced that more water is actually evaporated than during the inspiration of cold moist air. Of the total amount of moisture evaporated, Goodale estimated that the nasal mucous membrane contributes 23.6 gm. for each cubic meter of air or 67 per cent in cold dry air, 16.2 gm. or 55 per cent in cold moist air, 24.8 gm. or 68 per cent in warm dry air, and 17.5 gm. or 80 per cent in warm moist air. He found the relative humidity of air after passing the nasal chambers near the saturation point, that is, with

reference to its own temperature, but with reference to the temperature which it subsequently attains, it falls far short of saturation; for example, air at 28.5° C. with relative humidity of 92 per cent actually contains but 67 per cent of the moisture which it possesses when expired at a temperature of 34° C. and relative humidity of 100 per cent. While the nose nearly saturates the air it contributes only about two-thirds of the total amount of moisture evaporated by the respiratory tract.

The moisture thus extracted from the nasal mucous membrane represents a surprisingly large amount. Foster says, "In the 20,000 excursions of air through the nose each twenty-four hours, it supplies 2 quarts of fluid." Bloch believes, "The quantity of water taken up by the inspiratory air is, *cæteris paribus*, in inverse proportion to its rapidity." This also bears a definite relation to barometric pressure as noted before. Coakley and Kayser both estimate the amount of water secreted by the nose daily at 12 to 18 ounces, varying with the temperature and amount of moisture in the inspired air.

Goodale has calculated the amount of work done by the nose both in heating the air as well as vaporizing the water. This ranges from 3.4 gm. cal. for each 500 cc. of respired air in warm moist air to 11.05 gm. cal. in cold dry atmosphere. Four one-hundredths gram calories more work is done in a cold damp temperature (8.24) than in a warm dry temperature (8.20).

Bosworth has emphasized the fact that there is a delicate nervous mechanism which regulates the functioning of the nose. This control must be so delicately exercised as to meet not only daily, but even momentary, changes in the humidity and temperature of the inspired air. This nerve supply is through the cranial and thoracolumbar sympathetics. James is convinced that this vasotonic system which is Nature's protective mechanism can be kept fit by training. A changeable climate he says will bring this about. The nose in such a climate is efficient and has the exact supply of blood needed, the result of constant practise.

In the past there have been considerable speculation and varying opinions regarding the source of the nasal secretions. Bosworth believed there are no serous glands in the nose and that the mechanism by which water is poured out into the nasal chambers is in the so-called erectile tissue. The watery constituents of the blood transude the mucous membrane and appear on the tortuous surfaces of the turbinates. He does not explain how this is brought about. Wright[32] adds the idea that the elasticity, contractility, and tonicity of the stroma in which lie the capillaries, veins and venous sinuses must be properties regulating the amount of blood. He also affirms that at certain points each radical artery and vein stand in such a mutual relation that an increase in the diameter of the artery with its thick musculature must result in compression and

narrowing of the venous efferent vessels, thus mechanically contributing to the passive congestion of the capillaries and cavernous blood spaces of the erectile tissue.[33] As a result of this compression a transudation of serum from the vessels directly to the surface occurs.

Later[34] he thought it possible to see direct diapedesis of the white cells through the capillary walls and between the gland cells into the lumina of the acini. He thought it reasonable that in this way the bloodvessels may empty the serous and leukocytic elements of the blood directly into the glands. In sections he often observed the basal layer of epithelium broken by the eruption of leukocytes so that they frequently found their way to the surface. Wright[34] also noted the interesting fact that there is a thick network of capillaries around the ducts of the glands. A vasomotor dilatation of these capillaries would naturally result in considerable constriction of the gland outlets. This would cause the acini to dilate. As the vasomotor excitement subsides, the superficial capillaries cease to cause compression and a free vent is afforded the contents of the seromucous gland.

On the other hand, there is no special arrangement of the smooth muscle or elastic fibers around the fundus of the gland. While the gland has a regulating apparatus at its outlet, it has to depend on the pressure of the stroma around its fundus and on the general resiliency, tonicity and engorgement of the lymph spaces for the expulsion of its contents.

Fischer and others have shown the serious error in the commonly accepted view that the transudation of watery fluid from the bloodvessels is due to a heightened blood pressure. Fischer has demonstrated it to be a colloid-chemical phenomenon. Congestion or edema of the turbinates is due to the affinity of the stroma cells for the watery serum in the flowing blood of the vessels. This physiologic process is reversible, as shown by the turgescence and collapse of the turbinal tissue. Wright explains this colloid-chemical process by the fact that the lecithin of the nasal mucus, even though not water soluble, is capable of taking up water. This imbibition is regulated by the electrolytic salts which he thinks are probably derived from the vasomotor nerves.

Not much mention is made of the general distribution and elimination of the nasal secretion. Wright[34] tells of the secretions being carried to the pharynx in the gutters of the architecture, aided by the cilia. Coakley agrees in general with this statement, while Wood, Andrews, and Reed believe that the cilia always move toward the external orifices of the body rather than toward the pharynx.

Certain observations have been made regarding the nasal mucous membrane at different ages of life. In children the epithelium is columnar, whereas in adults it is mixed or flat; also the cilia in the

nose are lost in many places by the advent of adolescence, and the erectile tissue is only seen in its fullest extent after this time of life. Wright[32] found that at puberty there occurs a marked development and increase in the stroma and especially in its vascular mechanism, whereas in old age the erectile tissue atrophies. Douglas brought out the fact that although the old have nasal trouble, few complain of it. He thought that possibly as the system grows older, elimination is decreased and there is a lesser demand on the part of the inspired air for heat and moisture to satisfy the physiologic function of the respiratory tract.

Paulsen, Zwaardemaker, Franke and Rethi have shown experimentally that the smaller upper part of the nose is used in inspiration. Hofbauer has recently done experimental work to bear out this fact. He believes the air takes its course through the narrow upper part of the nose because of the horizontal placement of the nostrils forcing air vertically upward toward the bridge of the nose. During the recent war it was noted that people without external noses complained of the same symptoms as patients who had undergone tracheotomy.

That the normal nasal mucous membrane bears a very intimate relation to the rest of the body is evident from the frequency of rhinitis following chilling of the body or wetting of the feet. Spratt emphasized the fact that animals chilled by wetting the fur more readily succumbed to infections. Ridpath has gone so far as to say, "Located on or within the Schneiderian membrane, there is a reflex to practically every part of the body." In 1915, Andrews said that intranasal stimuli might produce coughing and sneezing, doubtless by the impulse being switched onto the vagus, which receives sensations from the pharynx, larynx, bronchi and lungs. Ridpath considers coughing, sneezing and lacrimation all physiologic nasal reflexes.

Brubaker attests that psychic states of an affective or emotional character may cause the nasal mucous membrane to swell up and secrete. Literature is notoriously sparse in regard to the relation of the mind to the nose.

Hagemann maintains that the mucous membrane of the upper respiratory tract is an eliminative organ for substances resulting from metabolism, including the toxins from constipation. Experimentation with drugs readily demonstrates that iodids and some other drugs are carried by the blood and lymph to the nasal mucous membrane.

Although rather commonly known, mention should be made of the definite physiologic relation of the nose and the sex organs. Schaeffer says, "Turgescence of the erectile tissue of the nasal fossæ may regularly accompany menstruation in women with normal nasal mucous membrane." Mention has been made of the physiologic activity of the nose at puberty.

Finally Tatum has, by plethysmographic experimentation, shown that nasal volume is influenced by pulmonary ventilation. When respiration is obstructed, there is a prompt enlargement of the nasal chambers; whereas overventilation results in vasodilatation in the nose.

Materials and Methods of this Study. Throughout these observations persons with apparently normal noses were observed. Ten persons in each of the first six decades of life were selected. Special attention was directed to the ages in the second decade before and after puberty. The nasal membrane in every case was carefully observed in each of the various atmospheric conditions noted below, so that a total of 240 observations were made. Not more than two noses were studied over the same period of time in order that an accurate mental picture could be carried between the examinations. Observations were made at ten-minute intervals or more frequently during changing conditions, and always over at least two-hour periods.

An attempt was made to secure uniform psychic influences by engaging the subjects in the same type of conversation, looking at pictures, or reading geographic studies during the intervals. In selecting the conditions under which to observe the reaction of the nasal mucous membrane, an attempt was made to supply every possible relation of temperature and humidity of the atmosphere which is ordinarily encountered: (1) Medium states of external air with a temperature of 13° to 18° C. and relative humidity of 50 to 60 per cent; (2) cold damp air with a temperature of 0° to 5° C. and relative humidity greater than 70 per cent; (3) warm dry air with a temperature of 20° to 27° C. and relative humidity less than 40 per cent; (4) warm moist air with a temperature of 20° to 27° C. and relative humidity greater than 70 per cent.

Cold dry air with a temperature of 5° C. and relative humidity less than 40 per cent as used by Goodale was purposely avoided because the United States Weather Bureau records for eighteen years show that the mean relative humidity in this part of the country during the coldest months was never below 67 per cent. This is also universally true to a lesser degree. Hygrometric tests performed during these observations also bear out the fact that the relative humidity in cold weather is surprisingly high, usually more than 75 per cent.

The atmospheric conditions of the experiment include the artificial climate in which we live eight months of the year as well as the hot rainy season.[30] It covers the changes from the hot dry air of our buildings during winter to the air outdoors, which may represent a change of 70° F. It also takes into consideration heat, humidity and stillness, which James considers the constituents of a bad atmosphere; and coolness, dryness and motion, the essentials of good ventilation.

In order to establish and regulate the various atmospheric

conditions, it was necessary to resort to mechanical and physical aids. These include electric and steam heat, steam, running water, saturated towels and electric fans. Some of the subjects were examined in the open air, but in order to bring about rapid changes, several rooms were required, in each of which one wall could be quickly removed. These rooms contained all of the above accessories.

In determining the relative humidity an hygrometer was used. This was the sling psychrometer issued by the United States Weather Bureau.[24] This instrument includes two mercury thermometers, the reservoir of one of which is covered with muslin. After the muslin is moistened the combined thermometers are rotated for two minutes. The evaporation from the muslin and consequent cooling of the bulb being proportional to the dryness of the air, the difference between the readings of the two thermometers is greatest when the air is dryest and zero when it is completely saturated. The same instrument was used for determining the temperature.

Results. Medium states of outside air with a temperature of from 13° to 18° C. and relative humidity of from 50 to 60 per cent may be regarded as optimal atmospheric conditions. Under these conditions every subject showed slight swelling of the turbinates, and in approximately 95 per cent the nasal secretions were scantily distributed over the nasal mucous membrane. There was a correspondingly large breathing space. These observations tend to agree with Goodale's calculations in which the least amount of work was done by the nose in warm, moist air.

The opposite extreme was observed in cold, damp air. There was a marked increase in the size of the turbinates and in the amount of the seromucus secreted. Many subjects showed definite turgescence of the turbinal structures. The nose apparently has much work to do in heating and moistening cold air.

Observations brought out the fact that in warm dry air the turbinates were considerably swollen, although perhaps a little less than in cold damp atmospheres. The nasal secretions were definitely reduced in amount. Here again the nose must have a definite function, which consists more in moistening than heating the inspired air, as it is already warm. The swollen turbinates probably also act as an adaptive reflex mechanism in preventing too free admission of the warm dry air. Many of the subjects experienced stuffiness in either side of the nose in this environment which was relieved by ventilation with fresh air. In warm moist atmospheres there was much less swelling of the turbinates than in warm dry air but more than in the optimal conditions. The secretions were equal in amount to those with optimal conditions.

During these observations attention was attracted by the bilateral waves of swelling and reduction in about 5 per cent of the

noses examined. These were very definite and did not disturb the relation of the two sides. Possibly the turbinates had adjusted themselves to their environment and hence had undergone bilateral diminution.

Observations lead to the belief that the apparent decrease in the size of the turbinates with forced inspiration is due merely to the rush of air against them, and *vice versa*.

In the absence of swelling the mucous membrane appears red or pink. When swollen, however, there is a change depending on the age of the subject. Every preadolescent examined, except two boys thirteen years old (possibly in early adolescence) had a pink mucous membrane, though definitely swollen. Following adolescence the turbinates when active appear turgescent. The mucous membrane is then pale and anemic looking. In 6 of the series of 240 observations the surface capillaries stood out clearly on the turgescent turbinates like telangiectatic vessels in the skin.

When subjected to varying environmental conditions the nasal mucous membrane showed a great variation in the rapidity of response in different individuals. In some cases the variation occurred in the same individual under similar conditions on different days, but in general, adolescents showed the most active mucous membrane. From adolescence until old age there was a progressive retardation in the response of this membrane. In many of the older subjects the turbinates were atrophic and appeared resistant to response and never changed as completely as in younger subjects.

In 1923, Lillie called attention to the idea of a cycle of reaction in the nose. He says, "The mucous membrane of one nasal cavity is filling to a point approaching obstruction while the other is throwing off its secretion."

Every nose examined in this series showed a definite fluctuation in the size of the turbinates even when conditions remained the same. In about 20 per cent of the cases there was fluctuation without a cycle of reaction, that is, one side of the nose was swelling and emptying without the opposite phase on the other side. This fluctuation varied considerably with environment and age of the subject.

A definite cycle of reaction was apparent in the remaining 80 per cent of the subjects. The turbinates on one side of the nose were filling while the other side was throwing off secretion. When the filling of the turbinates on one side had reached its maximum, the turbinates on the other side were completely empty, thus affording much breathing space. This cycle did not always take place to the same extent. Cold, damp atmosphere prompted more pronounced changes than the less provocative environments. In general it was observed that the optimal atmospheric conditions caused cycles of least degree, especially in older persons, in whom a rather superficial cycle of reaction was observed. It must also

be stated that the same nose responded differently at various times, under apparently the same conditions. No ready explanation for this offers itself.

These cycles of reaction in the nose occurred over varying lengths of time, ranging from fifty minutes to four hours. This includes both the phase of filling as well as the phase of emptying on the same side. In general more time was required for the cycle when marked swelling occurred, as there was a greater exchange of blood and lymph. On the other hand, less time was required under favorable conditions when the cycle was of less degree. The average time for a complete cycle under all the atmospheric conditions of the examinations was estimated to be two and one-half hours.

Subjects were also examined in sleeping postures because of the common complaint of nasal obstruction on the dependent side at night. It was observed that the distribution of the nasal vascular contents must be largely controlled by gravitation. The lower side nearly filled, or filled completely in every case and in less time than was required by the upright position. By turning the subject over, the other side could be made to swell. An average of only twenty-five minutes was necessary for the dependent side to attain its maximal size or swelling.

The nasal secretions over the mucous membrane which usually appeared in the form of seromucus bear a definite relation to the congestion of the turbinal structures. In cold air the secretion was abundant, in warm dry air it was less copious and in many cases it appeared dull and cloudy. The secretion was least abundant in moderate temperatures with relative humidity around 60 per cent. This close relation between the amount of the nasal secretion and turbinal congestion was further noted during the cycles of reaction. Except in 2 cases examined the swelling of the turbinates and the more abundant secretion occurred simultaneously, and *vice versa*.

During adolescence, an age of physiologic activity, the nasal secretions were found to be abundant. Excessive nasal secretion is a symptom complained of by many persons at that age. In old age and advanced middle life, the secretions were normally much reduced in amount. There was no uniformity of distribution of the nasal secretion. Frequently it was observed to form an even moist coat for the turbinates. Only 6 cases showed beads of secretion on the mucous membrane. This may be accounted for by the anatomic arrangement of the capillaries around the gland ducts. As noted before when capillaries dilate, the ducts are automatically obstructed, but when they reduce in size the glands empty themselves, and it was this phase which was observed in the form of beads. Two-thirds of the nasal cavities observed contained filaments and larger bands of seromucus between the septum and the turbinate bodies which were often formed within five minutes. After the secretions left the walls of the nose, they were seen collected over

the floors of the nasal cavities which form natural gutters running downward posteriorly to the nasopharynx.

In about 10 per cent of the cases there was definite débris about the vibrissæ of the nasal vestibules, and in at least half of the nasal cavities the secretions were discolored or contained fine débris.

Every subject examined in the lower temperatures showed moisture in the vestibules. This moisture was never observed in warmer air and could be produced by exposing the subject to cold air for five minutes. The logical explanation of this fact is that cooling the inspired air lowers its saturation point and some of its moisture must be precipitated. No lymph spaces or vascular spaces are found in the lining of the vestibules so that no transudation could take place there. Further, the fact that moisture occurs only in lower temperatures indicates that it must be the result of vaporization.

Conclusions. 1. The nose has three definite functions other than olfaction: to warm, moisten, and filter the inspired air.

2. The mechanism is the mucous membrane, the available surface of which is increased by turbinal turgescence.

3. The nose reacts differently under various environmental conditions and at different ages.

4. Most noses show a fairly definite cycle of reaction.

5. The following symptoms need not be due to pathologic conditions and can readily be explained as physiologic responses: Nasal obstruction in hot dry rooms, the watery nasal discharge in cold weather and during adolescence, the dropping back into the throat of secretions, often containing débris, and obstruction of the nose on the dependent side.

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ESSENTIAL HYPERTENSION.*

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Arterial hypertension constitutes one of the most puzzling and controversial problems of present day clinical medicine. This may be, to some extent, due to the fact that as expressed in mathematical terms it is comparatively speaking a new object of interest

* Address before the Buffalo Academy of Medicine, December 8, 1926.

which swam into our ken with the introduction of the clinical sphygmomanometer. Blood pressure studies have revealed an extraordinary thing little dreamed of in former times. It has been estimated on a basis of observations that 10 per cent of mankind over forty years of age subjected to this procedure have blood pressures elevated above the accepted standard of normal for their age group. This is probably a conservative estimate. Those among my hearers who are my medical contemporaries may be able to recall the fact that our familiarity with this phenomenon has developed during the past thirty years—since, in fact, we were first enabled to compute in mathematical terms the so-called arterial pressure. Previous to that time such knowledge of the condition as we possessed was of a general and indefinite character.

During the early days of clinical sphygmomanometry, the crudity of our technical equipment enabled us merely to estimate the systolic pressure. With improvement in instruments and methods, diastolic pressure in instrumental terms of accuracy became familiar and broadened our view so that it included peripheral as well as central, arteriolar as well as cardiac and aortic factors. With this came a better understanding of the mechanism at work to produce this interesting functional anomaly. Hard upon the heels of increasing clinical familiarity there followed attempts at clinical grouping and we find "arteriolar hypertension" spoken of as familiarly nowadays as "arterial hypertension" was a few years ago—whereas "malignant" and "benign," "chronic" and "fulminant" are terms the fascination of which certain writers appear unable to resist. Whether any classification now in vogue, even the simple one of "primary or essential" and "secondary" will stand is an open question. It is well to bear in mind that we are still in the early or clinical stage of our knowledge of high blood pressure. Theories abound, but facts are few. We know as yet practically nothing that is verifiable about its etiology and pathogenesis. We should consequently strive to keep our outlook free and not allow it to become prejudiced by any of the many theories and unsubstantiated claims now current.

With the development of our knowledge of high blood pressure largely based upon accumulated clinical experience, cases of hypertension have become divided into two main groups. One of these includes all instances where the elevated blood pressure appears in symptomatic association with nephritis or other obvious cause, and the second group comprises the large number of cases displaying high pressure without demonstrable kidney lesion or other primary organic factor. It will not do to draw too sharp a line of distinction between these two groups since it is only in perspective that one can feel absolutely sure to which one any individual case belongs. Despite the shortcomings of its descriptive adjective the designation "essential hypertension" has been widely adopted in this country

to cover the large group where the elevated pressure appears to be primary and the clinical course free from important extravascular contributions. It is with this type of hypertension that the present discussion will be concerned.

To solve the problem of the etiology of hypertension has proven one of the most fascinating preoccupations of clinical and laboratory research and has engaged the attention of many of the ablest investigators. Bright, the pioneer among this host of workers observing the enlarged heart and stiffened arteries of those dead of nephritis, assumed that these were the results of the presence in the blood and tissue fluids of some excrement material which the diseased kidneys failed to remove. This simple *a priori* explanation seemed to meet the requirements of the times, until the development of biochemistry turned the attention of investigators to the identification of the metabolic waste material that might in concentration cause such widespread circulatory effects. One after another the metabolites of the body were carefully investigated but no one of them nor any combination has as yet been, successfully linked with the causation of persistent elevation of blood pressure or with the production of the severe mechanical effects on heart and arteries. Despite the discouragements of the past, research along this line is still in active prosecution. The latest work of the kind, is that of Major who has shown that guanidin, one of the rarer nitrogenous waste bodies, is excreted with difficulty by the kidneys in hypertension cases and conversely that this substance when injected in certain concentration and at a certain rate directly into the circulation of animals is followed by a prompt and decided rise of blood pressure, in many instances persisting for three to four or even five hours. Major interpreted the evidence obtained as appearing to point to an action of guanidin on the vasomotor control of the arterioles and capillaries. Further developments in this research will be awaited with an interest that the disappointments of the past along lines of equal or greater promise should not prejudice.

Fifty years ago, attention was concentrated not upon biochemical research to detect the toxic material causing the elevated pressure, but on the biodynamic aspects of the problem, to discover by minute anatomic studies the mechanism by which it was brought about. Gull and Sutton described changes in the minuter vessels which they termed "arteriocapillary fibrosis" and which they assumed to be primary. To the peripheral obstruction these caused, they attributed the central rise of pressure. George Johnson, dealing with the same structural alterations, reached the directly opposite conclusion, that the blood pressure elevation was not the result but rather the cause of arteriolar fibrosis. This controversy is still open. The point has never been decided to the satisfaction of all as to which is the horse and which the cart in this matter. As time has gone on and studies of the minuter circulation have accumulated, it

becomes apparent that the view that hypertension is due to exaggerated resistance offered by organic narrowing of the arterioles is untenable, for a true generalized arteriolosclerosis does not exist in association with hypertension and therefore cannot be the cause of the latter. The latest anatomic studies, those of Fishberg,[1] did not disclose even in the most typical cases of essential hypertension an area of vascular involvement approaching in extent what would be necessary to account for the rise in blood pressure. Physiologic experiments have demonstrated long ago that any increased peripheral resistance in an organ or other vascular area is promptly offset by vasodilatation elsewhere so that general blood pressure is not disturbed thereby. Peripheral vascular narrowing would have to involve very extensive areas simultaneously before vasomotor control could prove inadequate to equalize pressure. Vascular alterations, on the contrary, appear to be practically always regional and furthermore not invariable or even constant in their distribution. They involve most frequently the arterioles of the kidneys and next in order of frequency the spleen, pancreas, liver, brain and heart, but by no means any one of these organs constantly. The great vascular areas of the muscular and cutaneous systems Fishberg found to be little, if at all, involved. If order of frequency were any criterion, it might then be assumed that arteriolosclerosis of the kidney is the cause of high blood pressure. This conclusion is difficult to establish, inasmuch as marked renal arteriolosclerosis often exists without high blood pressure and *per contra*, high blood pressure without renal arteriolosclerosis. The attempt has been made to attribute hypertension to sclerosis of the splanchnic vascular field (Hasenfeld and Hirsch), and more recently Bordley and Baker[2] undertake to demonstrate its causation on a basis of minute anatomic study of the arteriolar twigs in the brain stem of certain patients who during life had displayed a persistently elevated blood pressure. It is difficult to understand how any convincing demonstration of this or any other theory of the structural etiology of high blood pressure can be forthcoming, until the vexed question is settled as to whether arteriolar changes may not in fact be the result, rather than the cause, of the elevated pressure. The fact that vascular fibrotic changes appear maximal in one region or another may be purely fortuitous and without special etiologic significance in a process that is admittedly regional and variable.

On the clinical side, the etiology of arterial hypertension has run the gamut of the fads. Since biochemical research has failed to establish any significant connection between nitrogenous waste bodies and high blood pressure, certain clinicians, desperately clinging to the toxic theory, have darkly hinted that it is the result of intestinal autointoxication, whatever that term may imply. The endocrinologists have had their day, but their ingenuity has proved unequal to the task and except in certain broad generalizations has

failed to throw particular light on the problem. It was to be expected in view of the preoccupation of the clinic with focal infection that so elusive a thing as high blood pressure and chronic focal sepsis would be made to join hands. No convincing conjugation has been established, the argument of experience and clinical research failing to certify the union.

The mysterious world of tissue metabolism, having furnished no endogenous matter upon which the blame could reasonably be placed, man's environment has been searched for some exogenous factor that might be successfully implicated. Man's diet habits, hygienic disharmonies, nervous and emotional overstrain and many other items have been duly examined and while freely admitting that any one or all of these may undoubtedly aggravate the evil when once established it does not seem as yet clear that they act as primary causes. This matter of man's reactions to his environment and the effects that may come from conditions inherent in present-day civilization in bringing about cardiovascular disease is a subject that may profitably engage systematic study. An extraordinary phenomenon is the rapidity with which deaths from circulatory diseases have advanced to first place in mortality statistics. This advance has been so rapid that it cannot be accounted for on the score of greater discrimination in diagnosis or improved classification in the registration of deaths, nor can it be dismissed with the explanation that recent increases in average longevity carry on a larger proportion of mankind into the degenerative periods of life.

Cardiovascular disease is undoubtedly far more prevalent than even mortality statistics, striking as these are, would indicate. This may be inferred from such a statement as that made by Christian in reporting a series of blood pressure cases followed through to their termination. Of the number, 25 per cent died of causes that had no bearing whatsoever on the hypertension. Christian accordingly concludes that this type of invalid has one chance in four of living out his life despite high blood pressure and finally dying of something entirely unrelated thereto. It is obvious, if this inference be correct, that 25 per cent or thereabouts of this type of cardiovascular invalid does not appear in the mortality column for circulatory diseases. Moreover, no one will claim that every hypertensive case is recognized either during life or in death. It becomes apparent, I think, from these considerations that cardiovascular disease cannot be fully represented even in the present highly impressive mortality list. Judging from the copious literature on this condition in recent and contemporaneous American medical writings, it is difficult to escape the conviction that high blood pressure is especially prevalent in the United States. It would be interesting to compare statistically its incidence in European countries whose inhabitants although not unlike ours racially yet live in a somewhat

different social and economic environment. Perhaps even more important and significant might prove the knowledge of how the natives of primitive countries living closer to Nature and more dependent on natural phenomena fare in this matter. The relation between man and his environment is fundamental. This is a generality to which no one can take exception. The facts we must consider in arriving at any insight into a problem of this kind pertain to anthropology and anthropology is one of the earth sciences and with the earth sciences, to quote a high authority, the most important matter is geographical distribution. The study of distributions will bring us face to face with the fundamental aspects of human society and even of man himself, for not only do habits and customs change in response to variations in environment but so also do bodily traits and physical reactions to alterative factors of intense degree. Without the possession of statistical proof, all assumptions are hazardous but there certainly exist some grounds for the belief that in this present day and age and in our bountifully favored country man's environment has acquired some intolerable ingredient that is affecting him to his serious physical detriment. Light on this aspect of our problem will undoubtedly some day be forthcoming and it will probably be enlightening.

However this may prove to be, the fact remains that in the present state of our knowledge one thing and one thing only stands out clearly as beyond question of importance in the etiology of high blood pressure. I refer to the influence of heredity. This is one cause about which we need not argue, the relationship is clear. In a high percentage of cases the family history, when it can be secured in any satisfactory detail, yields a clear account of deaths of direct relatives from vascular disease in one of its forms—cerebral, cardiac or renal. Often the coincidence is very impressive. Very recently in my own experience, cerebral apoplexy claimed five males in two generations of one family and all at about the same age. Systematic studies on this relationship strikingly confirm clinical experience. Just how heredity acts it is impossible to say, and would be idle to speculate upon. Perhaps the handicap works through transmitted tendency to early arterial senility, possibly through inherited vasomotor defect, or it may be by means of some slant of metabolism which develops at early middle age in those predisposed by heredity. In whatever manner it operates, there can be no doubt of its predominating influence. It is well to ponder this fact since it introduces biologic considerations into an obscure problem.

The suggestion has been made that high blood pressure most frequently picks out a certain type of individual who is described by Moschowitz, the chief proponent of this idea, as obese, short-necked, slow and unathletic in bodily activity. Furthermore he lacks the ability to play either mentally or physically. Having stunted imagination but with terribly intense although narrow mental range,

he exhausts his potential in middle age and spends the balance of his life vainly seeking health. Undoubtedly this individual, as described, may be identified in the vascular clinic but he is merely one of a crowd. All types appear to contribute to the group, short and tall, thin and obese, active and slothful, gay and morose. If attributes common to all exist, they appear to be impersonal and biologic rather than personal and temperamental. For one thing, practically all who develop hypertension have approached the portals of middle life before any considerable elevation of pressure is manifest. If present much before the fortieth year, it is usually secondary to nephritis or some other appreciable cause. The sexes are about equally affected but are not equally distributed through age groups. More males develop the condition between the ages of forty and fifty years but that discrepancy is balanced by a relatively greater contribution from the female side during the succeeding decade. It may be that this is due to some obscure endocrine influence having to do with the sex hormones brought to bear by the occurrence of the menopause. After the age of sixty, more women than men are seen with high blood pressure, and this undoubtedly results from their far greater tolerance of the vascular strain. Men withstand elevated pressures less well than do women so that fewer enter the sixth and seventh decennial groups than is the case with women.

Another outstanding characteristic, having possible biologic significance developed by group study, is the factor of heredity already alluded to. My own conviction is that this is of far greater importance than we at present appreciate and I firmly believe that as time goes on and observations accumulate we will find that primary hypertension is an expression of some morbid physiologic slant on a basis of familial predisposition.

If we follow attentively the course of a case of essential hypertension from an early stage, we will usually find that the blood pressure is at first and for a considerable period moderate and that it fluctuates within a comparatively wide range without any apparent reason. It is strikingly responsive to psychic stimuli. Its labile character is shown by the manner in which the pressure varies if it is taken a number of times at intervals of five minutes with the patient resting quietly. Tixier states that it is rare for blood pressure to remain stationary for as long as five minutes. These shifts in the height of the pressure level affect both the systolic and diastolic values, although less pronounced at the diastolic end of the formula. This is always less variable than the systolic pressure. Such eccentric behavior of the pressure level may extend well throughout the clinical course, even up to the time when the heart begins to fail. Ordinarily these casual fluctuations are not registered by any noticeable variations in the patient's subjective sensations and are obscure in origin. Another and probably cognate observation is that during this labile stage vasodilator drugs, such as nitrites, produce a decided

although transitory effect on the pressure level, both systolic and diastolic. Incidental variations of marked degree are also observed to follow emotional and sensory stimuli. A very odd and interesting series of observations are reported by Fischer.[3] As a result of 270 blood pressure readings in an unselected series of 80 patients, it was found that a difference between the two sides of the body was the rule. In only 13 per cent of observations were the readings the same for the right and left arm, the differences amounting on occasion to as much as 40 mm. appearing in both systolic and diastolic values. This is confirmation of an occasional puzzling clinical finding and furnishes another proof, were one required, of the fluctuant nature of blood pressure.

One should be chary in making deductions in a matter so obscure but it appears to be a fair inference that there is a considerable functional element at work, obviously operating through nervous pathways. May it not be as good a surmise as any other that essential arterial hypertension is in its inception a vascular neurosis, that certain individuals possessing certain susceptibilities in their vascular responses transmitted by inheritance pass into a state of vasomotor instability as middle life approaches? What puts the mechanism out of gear may not be a single factor of endogenous origin but the combined effects of those exogenous or environmental influences which make up modern life as we know it. May primary high blood pressure not constitute a perverted biologic reaction to environmental disharmonies which the many can withstand, but the few handicapped by heredity cannot? We do not lack for analogies. Among other reactions of the kind may be numbered duodenal ulcer, diabetes, spastic constipation, nervous dyspepsia, to mention only a few. To the abdominal neuroses, the resemblance is striking. Compare the individual with an irritable autonomic nervous system. For years the victim of spastic constipation, which is his reaction to a misfit environment, he finally develops a colitis or falls a victim to ill-judged surgery. Opposite to him place the individual with a congenitally hypertensive vasomotor apparatus who at the point of greatest stress in life fulfills his destiny by developing a spastic vascular state, which gradually undermining the structural integrity of his cardiovascular system leads finally to cardiac failure or the rupture of a cerebral artery.

If this theory be near the truth, it is in reality a doctrine of predestination, implying that the hypertensive cardiovascular invalid is foredoomed by inborn susceptibility inherent in his germ plasm to develop this especial reaction, if the conditions of his life and environment prove unfavorable to his weakness. No matter how attractive a theory may appear, it cannot be given any standing unless it seems to fit reasonably well the facts of the case. I have discussed the factor of heredity now generally recognized and acknowledged and have touched upon the influence of environment

and also the highly suggestive character of the vascular manifestations during the initial stages of development. When we turn to the practical clinical aspects of the problem, we find certain facts born of experience which appear to lend some support to the theory. Any thoughtful observer who has had much to do with the treatment of primary high blood pressure will, I feel sure, support me in the statement that it is only in the stage of early development that we can accomplish any great control of the condition. Even at that stage it is only by means of a careful painstaking inquiry into the patient's habits and environment and a radical correction of disharmonies and eradication of harmful emotional and sensory stimuli that we can retard its progress. Once the condition has become firmly established it pursues its life history undeviatingly. The extent to which control will be effective does not depend upon drug treatment or specific therapy, but upon whether the patient is willing to take advice and adopt the modifications of his personal hygiene appropriate to his disability.

It is not necessary to dwell upon the symptomatology of essential hypertension. During the early stage, there are few or no subjective symptoms and its existence is usually accidentally revealed. The systolic pressure is not high and varies greatly from day to day and the diastolic is but slightly elevated. There follows a period more or less prolonged when compensation is perfect and the patient in the main remains in satisfactory bodily comfort. During this interval, lasting often for months or years, the elevated pressure remains merely an object of more or less apprehensive interest to both patient and physician, the degree of elevation meanwhile undergoing steady but slow increase on both systolic and diastolic sides. It is a puzzling matter to decide how best to place the patient's problem before him. Understanding the predicament toward which the patient is slowly but surely progressing, one is impelled by the spirit of service to frankly and forcibly state the demands of the situation and the penalties that follow on neglect. This involves a certain amount of prognosis, always a hazardous venture in so chronic a malady. Counter to the apprehension of the informed physician there is often opposed the subjective well-being of the patient, who may feel secure in his ability to carry on and discounts in a spirit of scepticism the warnings given him. Furthermore, there is often a restraint imposed by our unwillingness to alarm unduly, for worry and depression are enemies to be reckoned with. Compromises forced by economic and other considerations are necessary and the matter presently becomes much involved. However definite and well understood the principles of treatment may be, they can rarely be carried out without modification to meet the necessities. Each case is an individual problem involving painstaking but leisurely education of the patient. The suggestion has been made by Norris that the hypertension patient be sent to sanitoria or other suitably

adapted institutions, where during intervals sufficiently long to insure results he will be instructed in a new personal hygiene suited to his altered circulatory state. Such a plan might be adopted with patients able to command the time and means necessary but their number must of necessity prove but a small percentage of individuals afflicted with high blood pressure. With the vast majority instruction must come from their personal physicians. What may be accomplished in this direction can only be brought about by a thorough understanding and coöperation between patient and physician. We should in this matter seek to duplicate the practice followed in the modern treatment of diabetes and tuberculosis.

Hypertension is a malady that in its development affects the bloodflow generally and consequently the function of all the internal organs more or less. Because of their extreme dependence on adequate blood supply, the heart, the brain and the kidneys display the greatest disturbance of function. Clinical manifestations involving one or more of these organs develop in every case of hypertension as it advances, although many times it is difficult to decide which organ is more severely affected. We should not wait for gross manifestations such as edema, angina, or cerebral disturbance, to develop. We should watch very carefully for the earliest evidence of progressive organ involvement. Intensive study is indicated. In periodic consultations, we should be on the watch for significant developments. The two most frequent causes of disability or death are cerebral hemorrhage and heart failure. These two practically cover the direct mortality from hypertension. Deaths from uremia are comparatively infrequent. In Christian's statistics 25 per cent died of cerebral lesions, 32 per cent of cardiac failure and 4.5 per cent of uremia. This is probably a fair representation of the average.

There exists no single criterion that will enable one to predict much in advance of the event when one of these results is impending. The height of the blood pressure cannot be trusted to foretell it, unless perhaps it be the diastolic level. A pressure of 130 mm. or over on the diastolic side is a wearing strain that neither heart nor artery is apt to tolerate for long periods of time. On the other hand, extravagant heights of systolic pressure are often borne tolerantly. The determining factor in prognosis is not then necessarily the blood pressure record but the patient's organ resistance—the ability of his heart and cerebral arteries to stand the strain. This all-important factor is unfortunately not determinable, as is the blood pressure, in mathematical terms. Clinical manifestations of functional decline announce to the attentive observer what may be expected. The physician's usefulness is proportional to his ability properly to appreciate and interpret such indications. Every patient with persistent hypertension is a potential cardiopath. If he escapes apoplexy and death from intercurrent illness, he will

eventually succumb to some form of heart failure. Aside from myocardial fibrosis resulting from associated coronary disease the failing heart of hypertension shows less structural change than would be expected. It is more "heart defeat" than "heart failure," cardiac decompensation being more the result of increased functional load than of myocardial degeneration. This is shown by Fishberg's recent anatomic studies in which the arterioles of the myocardium were found involved very infrequently. Since the hypertensive heart fails from fatigue, there should be some way of preventing or at least postponing this development. If we are to accomplish anything in this direction, we must be keenly on the alert for the earliest evidence of progressive muscle deficiency. These are nearly always subjective in character and not necessarily such as to direct attention especially to the heart. The patient may remark that he has observed a certain decline in the efficiency of his perceptive faculties so that he is less keen than he was. He lacks the normal healthy feeling of refreshment after a good night's rest. He confesses to uncharacteristic emotional instability, is less able to tolerate tobacco or is inordinately depressed after coitus. More definite and suggestive are increasing dyspnea and fatigue after moderate effort, rapid pulse, palpitation, postprandial oppression, vertigo on sudden alterations of body posture, pain and constriction in the chest, and so forth. He may assert that his discomforts, when referred to the chest, are relieved by belching and consequently ascribes them to indigestion or errors in diet. Recurrent premature contractions are highly suggestive, especially if they are increased by effort. Most significant of all is a permanent increase in heart rate. Other things being equal, a change from the deliberate, slow and measured heart beat ordinarily present in high blood pressure to one persistently more rapid signifies the advent of myocardial insufficiency. It is a fair presumption that this rapid rhythm represents an effort on the part of the ventricle to compensate by increase of stroke for reduced volume output. Progressive elevation of diastolic pressure is to be watched with the greatest concern and when observed, the urine, blood nitrogen derivatives and ocular fundi should be carefully studied. Decline of systolic pressure, if not attributable to therapeutic measures and if associated with increasing subjective discomfort, possesses unfavorable significance, pointing to myocardial exhaustion. Edema, alternating pulse, gallop rhythm, nocturnal asthma need no emphasis as to their implication. Cerebral developments are less easy to foretell. Failure of mental alertness, persistent occipital headaches, vertigo, transient disturbance of speech, memory or vision, retinal hemorrhages are among significant warnings. The urine should be analyzed at regular intervals and a kidney function test or blood nitrogen estimation made when indicated and at least twice a year as a routine, in order that uremia may not creep in unawares.

The treatment of the hypertensive invalid involves many considerations. Of its very essence is the element of time. The malady once developed lasts for the balance of life which may extend over many years. This fact imposes upon us a policy of conservatism under the operation of the golden rule. Life's responsibilities under ordinary economic conditions being what they are, we should endeavor to accomplish our purpose with the minimum restriction of and interference with the general activities of the body. There is no problem in clinical medicine that calls for greater patience and therapeutic ingenuity. Once familiar with the philosophy of the situation and with the principles of treatment, the way is clear. Certain details of treatment call for somewhat extended discussion.

Diet therapy in essential arterial hypertension, so far as it has been specialized, is predicated on the old and no longer tenable interpretation of hypertension as an associate condition or consequence of chronic nephritis. This applies particularly to the principles of protein restriction and of salt privation. In the great majority of cases of this form of high blood pressure, there is no demonstrable decline in the excretory efficiency of the kidneys. With normally functioning kidneys, it is consequently difficult to regard these diet practices as rational procedures. Aside from clinical logic based on physiologic considerations, the results of experimental research fail to justify either practice. Strouse and Mosenthal, in the case of strict protein restriction, and O'Hare and Walker, Mosenthal and others, in the matter of salt privation, appear to have knocked the props out from under the proponents of both methods. Moreover, as Allbutt points out, if high blood pressure is the result of some twist of metabolism, or if the biologic interpretation of hypertension suggested in this discussion be given any credence, it follows that the strict specialized diet is merely groping in the dark. As a counter to adverse criticism, the claim may be entered that the enforcement of both low-protein and salt-free diets do in many cases result in a decline in blood pressure. In rebuttal, it may be pointed out that both these forms of diet constitute in reality systems of underfeeding and that should pressures fall during their enforcement, nothing is proved for this result may be merely an indirect and not a specific effect but due in fact to a certain amount of undernutrition and secondary anemia resulting from subnormal food intake. All privation diets strictly enforced result in depletion and the low-protein and salt-free régimes should, in my judgment, take their place along with sweating and purging as methods not properly speaking for the lowering of blood pressure but for lowering general vitality. Such incidental decline of pressures as may be effected should not be misinterpreted and should be watched with concern as it may not result to the eventual well-being of the patient. This statement is not meant to imply that diets strict to the point of privation may not at times prove beneficial to certain of these

patients. A large percentage of hypertension patients are more or less obese. Vaquez refers to a "hypertension de luxe" occurring in heavy feeders. It is well known that the chief causes of death in overweight persons are in order apoplexy, heart failure, diabetes and nephritis. These types of patients will benefit by underfeeding whether enforced by either qualitative or quantitative methods. Faber's tables[4] show that, as a rule, with the treatment for obesity there occurred a fall in blood pressure—a loss of 8 to 16 pounds being associated on an average with a drop of from 15 to 30 mm. in systolic pressure. With respect to the strict low-protein diet, it may be pointed out that abnormally high carbohydrate and fat intake is necessary, and increase of body weight and incidentally perhaps of blood pressure without increase of efficiency may leave the patient worse off than he was before. With thin patients and those of standard weight with normally acting kidneys, it is difficult to see what good can be accomplished by subcaloric feeding. Aside from its harmful effect on the morale of the patient, it may not, in the long view work out to the advantage of his vascular condition. The closest attention should be given to enforcing the principles of diet moderation and the avoidance of all excess in eating, but except under special circumstances or to meet some definite indication, such as obesity, the practice of dietary depletion should not be enforced without a careful checking of its effect from time to time. The suggestion of Benedict may be adopted of regulating the degree and duration of the privation diet according to the hemoglobin index, which should not be allowed to fall below 80 per cent. What has been said about depletion by diet applies also to the employment of sweating and purgation. There may appropriately be included at this point some reference to depletion by venesection. Bleeding is an ancient therapeutic measure in this condition now generally discredited. Perhaps the condemnation of the practice has been unwarrantably severe. Purely as a matter of personal experience, I would regret to abandon it entirely in high blood pressure. In the plethoric individual with threatened heart failure of the type known as "high blood pressure stasis,"[5] a good bleeding will sometimes postpone the breakdown. In the presence of apoplexy prodromes, venesection may serve to tide over the crisis. The reduction of pressure, especially diastolic pressure, resulting from a free abstraction of blood may last for several days. In addition to its emergency use, there is something to be said for the employment of venesection repeatedly carried out to a moderate depletion at appropriate intervals in plethoric cases. This applies particularly to individuals with blood counts above normal. These cases have been designated "polycythemia hypertonica" by Giesböck and may be identified by their ruddy apoplectic appearance and blood count over 5,000,000.

Undoubtedly every hypertension patient is a cardiopath in the making. Study of the mortality tables supports this statement.

The largest proportion of these patients die of heart failure in one of its forms. The advent of impaired cardiac reserve does not necessarily bear any relationship to the individual's appearance of good health nor to the height of his blood pressure unless it be his diastolic pressure. Not a few patients develop the discomforts of coronary sclerosis while still appearing in robust health. An important question to be decided is whether we should wait for signs of warning to commence measures of heart conservation or whether we should institute a protective policy in advance. This is an open question, with arguments on both sides. To treat a hypertension patient who boasts of his efficiency and who aside from the high pressure appears to have a normal circulation, as though he were a sclerotic cardiopath seems unfair to say the least. On the other hand, the long view informs us of what is inevitably in store for him. Certain measures are applicable to all cases and the benefit they confer is obvious. Nervous tension, worry and excitement increase vascular spasm; consequently these individuals should invariably be cautioned against such things with an insistance that will leave no doubt in their minds. Meals elevate blood pressure and augment heart load. In Mosenthal and Shortt's studies, it was noted that the greatest drop in pressure usually manifested itself well within half an hour after lying down and that the subsequent blood pressure when sitting or upright position was resumed often did not return to the initial level for a considerable period. This shows that a half-hour rest or nap after meals systematically practised may have far-reaching consequences. Postprandial rest and relaxation, both physical and mental, should be insisted upon from the earliest stages of high blood pressure. As the case advances, greater and greater emphasis should be placed upon this invaluable therapeutic aid. Regular and long hours of sleep, avoidance of sudden strain and of activities leading to excessive fatigue should be insisted upon. Periodic vacations, preferably with change of scene and interest, should be recommended. With the advent of dyspnea following meals or usual activity, greater restrictions should be enforced. Every other week-end in bed is an excellent practice for patients engaged in active business and one of the very best therapeutic measures we have is a week or two in bed with business excluded four times a year as a routine. The fact that pressures rise again to former levels after the patient gets about does not disqualify the procedure. For a time at least, the strain has been relieved and circulatory reserve is improved thereby.

With the advent of the asthenic stage or period of cardiac insufficiency active therapeutic control becomes necessary. The blood pressure record cannot be relied upon to furnish the index of heart fatigue. Myocardial exhaustion may undoubtedly let the pressure down and a sinister significance attaches to a spontaneously falling systolic pressure, especially if accompanied by an increase in pulse

rate, arrhythmia or other evidence of cardiac embarrassment. It is well to bear in mind, however, that coincidently with ventricular exhaustion subjective symptoms may temporarily improve. There may be less headache, less nervousness as the systolic pressure falls, but the appearance of venous stasis or edema shows which way the wind is blowing. An important fact is that the heart may fail without decline in pressure and even with a rising pressure. The last ounce of reserve power may be put forth by the heart muscle against high peripheral obstruction in maintaining mass movement of the blood. It is the diastolic excess that aggravates the evil. More attention should be given to this element of blood pressure than to the systolic, the prognosis becoming increasingly grave as the diastolic mounts. As soon as it is apparent that the heart is yielding to the overload, strict bodily recumbency should be enforced. In no other manner may the load be eased and reserve restored. Combined with rest, more careful control of diet and freer elimination become advisable. Resumption of activity should be gradual and under strict supervision. Edema in essential hypertension is almost always cardiac and not renal in origin. If there is reason to distrust the heart's ability even with the help of digitalis to take care of the dropsy, the circulatory diuretics may be employed. Theobromin, theocin or theophyllin may prove effective. If these do not suffice, euphyllin may be tried and next in order salyrgin or novasurol. I have had many occasions to be pleased with the action of novasurol. It is a powerful agent in dealing with cardiac dropsy. It may prove more effective when given intravenously than by the ordinary intramuscular technique. With ammonium or calcium chlorid it may act more vigorously than when given alone and associated digitalis administration is helpful to its action.

Our last therapeutic stand in the failing heart of hypertension is digitalis. Although perhaps less effective on the whole than in other types of heart failure it should always be given a patient trial, using a carefully selected standardized preparation of the drug. When the necessity for stimulation is urgent, a sterile solution administered by vein may for a few doses be indicated. In ordinary gradual ventricular failure, the method should be more conservative. Thorough digitalization is ordinarily not indicated and had better not be attempted. Having determined the optimal dosage this should be continued as long as need exists or response is secured. It may be necessary to employ the drug more or less permanently. The failing heart of high blood pressure working ever on the verge of breakdown cannot be trusted for very long at a time to take care of itself without support.

I shall have little to say regarding special methods of treatment of high blood pressure. There have been many such advocated but none has stood the tests of time and trial. Perhaps we have not far to seek for an explanation. Hypertension is a progressive

process and one of the most chronic in its clinical development. Organic secondaries develop very slowly and become apparent ordinarily only after the lapse of years. Although at the outset the perversion seems to be a functional one, it is possessed of two leading characteristics which are more or less contradictory, that is, inveteracy and variability. Once established, hypertension proceeds inveterately at its own leisurely pace, gradually gaining in momentum as time goes on as though performing a set biologic task. This inherent character of hypertension foredooms efforts at cure and raises obstacles to control that are rarely surmounted. Variability is an equally characteristic attribute and the failure to give it due consideration has led many an honest observer into false therapeutic deductions. Cannon states, and this reflects general opinion, that the main factors determining the degree of arterial pressure are first, the energy of the heart, as measured by the volume of blood pumped into the system at a given time and second, the degree of resistance present in the terminal part of the arterial system at the same time. Both the heart action and the tonus of the peripheral arterioles, but especially the latter, are extremely sensitive to environmental factors, especially to stimuli brought to bear by emotional phases of daily experience. By these means are brought about the marked variations in pressure that are so characteristic and of such great clinical importance. It is obviously true that in order to appraise the genuine effect of any measure of therapy, the observer must be acquainted with the course of the untreated disease and it is only when the results of his therapy depart radically from the natural expected phenomena that he is justified in drawing conclusions. Although variability is a well-known characteristic of hypertension, that is freely acknowledged in all theoretical considerations of the subject, it is rarely taken into account when it comes to clinical observation and research. The very large number of therapeutic fiascos in essential hypertension may be laid at the door of neglect of this precaution. Lack of knowledge of or indifference to the natural history of the malady combined with failure to take into account the hopeful psychology surrounding all therapeutic experiment in chronic disease prepare a trap for the feet of the unwary.

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DIGITALIS IN PNEUMONIA.*

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Introduction. The question of the advisability of using digitalis as a therapeutic agent in the treatment of pneumonia, is one that long has been a subject of controversy. Schmiedeberg[1] in a résumé of the literature prior to 1883, notes that Ferrier recommended digitalis as early as the end of the eighteenth century as a substitute for phlebotomy in slowing the pulse. Currie (1804) reintroduced it after nearly half a century of disuse. Schmiedeberg concluded that the subject was still open to question.

In more recent years clinicians have differed radically in their opinions of the efficacy of digitalis in the treatment of pneumonia. Mackenzie[2] feels that it is of little benefit. Hare[3] is not enthusiastic, while Carhart[4] believes that the use of digitalis in the first and second stages of pneumonia is one of the causes of the large death rate. Brunton[5] finds that digitalis at a high temperature completely loses its power of slowing the heart through the vagus. Many consider that digitalis is only justified in those cases of pneumonia where auricular fibrillation or cardiac failure are present. Hart[6] is of this opinion. Christian[7] says: "I see no advantage of the routine use of digitalis in pneumonia. . . . If auricular fibrillation develops, or cardiac decompensation is present, digitalis is very useful." Gibson[8] expresses similar views. In 1921 White[9] in discussing the heart in infectious disease said: "We are a people of fads and fancies, and it seems to me that just at present the fad is digitalis as a routine to avert circulatory failure in infectious disease." He believed that unless the drug has a real therapeutic effect in pneumonia it might be unwise to add the toxic action of large doses of digitalis to that of the disease.

In a carefully controlled series of cases Cohn and Jamieson[10] conclude that: "Digitalis acts during the febrile period of pneumonia and produces a beneficial, possibly a life saving effect, in cases of auricular irregularity (fibrillation and flutter). Whatever beneficial action it has on the function of the normally beating heart, may be expected from its use in the febrile heart in pneumonia." Brooks and Carroll[11] say: "It is our custom to give digitalis at the moment the diagnosis is made, or even when it is highly suspicious." Bishop[12] is equally enthusiastic. Romberg[13]

* Read before the New England Heart Association, May 27, 1926.

gives digitalis to all pneumonia patients suffering from heart disease, as soon as the diagnosis is made. Phillips, Bliss and Stone,[14] from the study of a series of 871 cases believe that "the use of a standardized tincture of digitalis in sufficient dosage to produce physiologic effect, is responsible for a decrease of deaths not associated with empyema or other septic complications." One of the same authors, Stone,[15] in a still larger series, draws similar conclusions which are of considerable interest, especially in view of the large number of cases. They would be more convincing if the two groups of cases—those given full doses of digitalis and those not given such doses—had covered the same period of time, since there may be a wide range of mortality percentages during different epidemics of pneumonia and also during different stages of the same epidemic. It is also often very difficult to separate circulatory failure from cardiac failure in such statistics, although if digitalis is really effective, it matters little whether the failure is cardiac or of other circulatory origin.

Present Observations. With the hope that added data might supply more definite evidence upon which to draw conclusions, the records of a number of cases at the Massachusetts General Hospital have been examined. To this end, a series was selected representing all of the 221 cases of lobar pneumonia treated upon the adult medical wards of the hospital during the five years from January of 1921 through December of 1925. The length of this period helps to rule out any variations due to epidemics or to annual changes which might be encountered in a shorter time interval. No selective factors were considered other than a clear-cut clinical or pathologic diagnosis of lobar pneumonia.

An additional group of 87 patients admitted to the Children's ward during the same period, was disregarded because over 98 per cent had received no digitalis. The percentage of mortality among these children was likewise materially lower than was found in the group with corresponding medication in the older series.

Of the 221 cases under critical examination, 110 or 49.8 per cent received no digitalis, while 111 or 50.2 per cent were given various amounts of the drug. The mortality in the former group was 16 per cent, while that in the latter was 39.6 per cent, or nearly two and a half times as great. In an effort to determine the relative seriousness of the cases in the two groups, a study was made of the number that had complications serious enough to introduce added factors which might influence prognosis, apart from the original pneumonic process. Under this heading were included such conditions as lung abscess, septicemia, empyema, etc. In the two groups the percentages were somewhat similar, there being 50 per cent of complications in those patients who received no digitalis and 54 per cent in the other series. Fifty per cent of the cases, both with and without digitalis, were put upon the danger

list within forty-eight hours of their entry into the hospital. A comparison of the age incidence showed that the average age of the patients without digitalis was thirty-nine years, while that of the patients with digitalis medication was forty-eight years. Of those who died the averages were thirty-nine years for the former and forty-six years for the latter.

Study was made of the type of pneumonia in all of the cases, with special reference to the patients who died. It was found that the mortality among those who were typed was almost equally divided among the four groups.

Attention was next turned to those cases which had been given digitalis. Of these, 40 or 36 per cent appeared to have been actually digitalized. Digitalization was computed upon the basis of 1½ gr. for every 10 pounds of body weight, a figure slightly lower than that of Hatcher and Eggleston; but the one at present in use as a very satisfactory clinical basis for digitalization in this hospital. The average dose per patient was 36.5 gr. administered in large part in the form of 1½-gr. pills in the course of two, three or four days.

The remaining 71 (64 per cent) received varying amounts of the drug administered over varying intervals of time.

These two groups, the digitalized and the nondigitalized, were subjected to the same inquiries. It was found that the percentages of complications and danger-list patients were similar. The average ages for the series and for the deaths were forty-two and sixty-two years respectively for the former group, and thirty-eight and forty-four for the latter. The mortality, however, was but 10 per cent in those cases which had been digitalized, and 56 per cent among those patients who had received casual digitalis medication.

Study of the nondigitalized group showed that digitalis had been administered in the most haphazard fashion. The varieties in amount and time of dosage were so numerous that no figures were obtainable. In some cases one ampule of digifolin would be given as the patient came into the ward, to be followed by no further digitalis medication. In practically 50 per cent of the cases, small doses of digitalis were administered when the patient was *in extremis* in an apparent effort to avert a fatal termination. While such doses as 1½ or 3 gr. had no appreciable effect upon these patients, their administration served to place a large number of ultimately fatal cases in the class receiving some digitalis medication, and thereby nearly doubled the mortality in this particular group. Upon occasion, the drug was tried intermittently at intervals of a week, or given daily in 1½-gr. doses without digitalization as a "supportive measure." So far as could be observed, this medication was without benefit.

Nearly all of the cases received various other forms of medication aside from digitalis. Morphin and codein were the most consistently used, with various so-called stimulants, oxygen and anti-

pneumococcus serum as occasional factors. The latter was given in comparatively few cases, as patients were seldom received in the wards early enough in the course of the disease to make its administration worth while. Attention was given to the relative frequency and times of crises in the various groups, but as it was found that the average time for starting digitalis was not until the sixth day of illness the findings were considered irrelevant. Six cases, or slightly less than 3 per cent, presented questionable evidence of organic heart disease upon entrance, but neither the treatment nor the outcome seemed consistent enough to influence the various group figures.

In a study of this nature, it must be realized that the many variants which necessarily enter the picture, demand the utmost caution in the interpretation of findings. Nothing but a very extensive series of carefully selected cases could be considered conclusive. From the foregoing data it would, however, seem fair to point out certain facts and conclusions which follow.

Summary and Conclusions. 1. In a group of 221 unselected cases of lobar pneumonia in adults, approximately one-half received digitalis medication in varying amounts, the other half, none at all. Those who received digitalis showed a mortality two and a half times that of those who received none.

2. The patients receiving digitalis were divided into those who were digitalized and those who were not. The digitalized patients showed a mortality only five-eighths as high as those who were given no digitalis medication whatever. Those receiving nondigitalizing doses showed a mortality three and a half times as high as those without any digitalis.

3. In the undigitalized group digitalis was administered unsystematically in many instances, being used as a last resort in about one-half of the cases at a time when they were very seriously ill.

4. In the groups here considered, among which the percentages of complications and danger list patients is very similar, the lowest percentage of mortality was found in those patients who were digitalized, and next in those who received no digitalis.

5. The definitely higher mortality among those cases receiving nondigitalizing doses should discourage this type of administration. If the drug is to be used, full digitalization should be accomplished.

6. It appears that the systematic administration of digitalis in digitalizing doses may have been of benefit in this series of cases.

7. No untoward effects from a toxic action of digitalis in the present series of cases were observed.

8. Larger series more carefully controlled than heretofore as to age, severity both of epidemic and of individual illness, complications, and amount of digitalis given, must be assembled before conclusive evidence can be obtained as to the value of digitalis in pneumonia. The data presented here, as in the case of Stone's

series, do suggest that digitalis is of value in pneumonia when given in sufficient dosage; the cases, however, are inadequate in number to prove the matter.

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REVIEWS.

A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners. By Oliver S. Ormsby, M.D. Third edition, thoroughly revised. Pp. 1262; 521 illus-illustrations and 3 colored plates. Philadelphia: Lea & Febiger, 1927. Price, $11.00.

This volume, the third edition of one of the best-known and most valuable texts in the field of American dermatology, satisfactorily maintains the excellent tradition of its predecessors and brings dermatologic knowledge up to date. The medical contacts of dermatology in the field of constitutional disease receive unusually satisfactory attention, and valuable bibliographic reference makes possible the pursuit of further knowledge for those concerned with other than local aspects. The diagnosis and treatment of syphilis is discussed with unusual completeness and intelligence. The illustrations are admirable, and the press and half-tone work a credit to the publishers. The edition easily maintains the distinguished reputation of its author. J. S.

Dudley Allen Sargent: An Autobiography. Edited by Ledyard W. Sargent; with an Introduction by R. Tait MacKenzie, M.D. Pp. 221; 1 illustration. Philadelphia: Lea & Febiger, 1927. Price, $2.00.

An interesting autobiography of a pioneer in physical education, who happily lived long enough to see much of his labor bear ripe fruit. To a Harvard man the near half century that he spent so profitably at Cambridge may seem scantily represented, but there will be compensations in the fuller treatment of his earlier career. The sympathetic introduction by another "combination of the scientist and artist" is also welcome. E. K.

The International Medical Annual. A Year-book of Treatment and Practitioner's Index. Pp. 560; 81 plates and 77 illustrations. New York: William Wood & Co., 1927. Price, $4.00.

The 1927 volume representing the forty-fifth year of this publication is more profusely and beautifully illustrated than previous

volumes. The new developments in medicine and surgery are dealt with in the usual concise and adequate manner. On the whole this is by far the best number of the International Medical Annual which has reached the reviewer's hands. J. A.

EXAMINATION OF CHILDREN BY CLINICAL AND LABORATORY METHODS. By ABRAHAM LEVINSON, B.S., M.D., Associate in Pediatrics, Northwestern University Medical School; Attending Physician, Children's Department, Cook County Hospital, Chicago; Attending Pediatrician, Sarah Morris Hospital for Children, Chicago; Attending Pediatrician, Mt. Sinai Hospital, Chicago. Second edition. Pp. 192; 85 illustrations. St. Louis: The C. V. Mosby Company, 1927. Price, $3.50.

THIS book in its second edition has benefited by enlargement and more orderly arrangement. The particulars of technique necessary in pediatric diagnosis are clearly described. Methods of obtaining specimens and the more frequent laboratory methods are explained in proper detail. Tables of normal values and the variations in these due to disease are generously supplied. The book contains a fund of information in a readily available form, and for this reason is an excellent handbook for the children's ward or practitioner's desk. J. S.

POSTENCEPHALITIC RESPIRATORY DISORDERS. By SMITH ELY JELLIFFE, M.D. Pp. 135; 28 illustrations. New York and Washington: Nervous and Mental Disease Publishing Company, 1927. Price, $2.50.

WITH his usual graceful style so familiar to us, this writer supplies a comprehensive historical résumé and then offers two case reports. One is that of a young man whose numerous diagnoses included hysteria, dementia precox, high-grade imbecility and petit mal, and who even without his encephalitis was said to be predestined to mental decay. The author, through Freudian psychoanalysis, restored his mentality and which had continued normal to the time of writing, eighteen months. N. Y.

INTRACRANIAL TUMORS AND SOME ERRORS IN THEIR DIAGNOSIS. By SIR JAMES PURVES-STEWART, Senior Physician to Westminister Hospital. Pp. 206; 71 illustrations. London: Oxford University Press, 1927.

THIS monograph is limited to the writer's personal observations in 117 anatomically verified intracranial tumors. To these are added

4 cases of gross errors where clinical data indicated tumor but which necropsy proved incorrect: (1) Multiple sclerosis; (2) serous meningitis with internal hydrocephalus following measles; (3) serous meningitis with hydrocephalus perhaps following measles; (4) pachymeningitis hemorrhagica with two subdural hemorrhages over the frontal lobes. The tumors were distributed as follows: 25 per cent each in the frontal lobes and cerebellum; 19 per cent in the parietal, occipital and temporal lobes; 7 per cent of the pituitary and 24 per cent in other regions. An excellent contribution.

N. Y.

BIRTH INJURIES OF THE CENTRAL NERVOUS SYSTEM. Part I—Cerebral Birth Injuries by FRANK R. FORD, M.D., Johns Hopkins Hospital. Part II—Cord Birth Injuries by BRONSON CROTHERS, M.D., and MARIAN C. PUTNAM, M.D., Harvard Medical School. Pp. 164; 60 illustrations. Baltimore: The Williams & Wilkins Company, 1927. Price, $4.00.

FROM available material it appears that most congenital diplegias, paraplegias, hemiplegias and monoplegias result from birth injuries. That they are only an exceptional cause of chronic hydrocephalus. That they cause 2 or 3 per cent of epilepsies. That they rarely cause mental defects of pronounced degree.

Cord injuries resulting from obstetrical accidents cause flaccid paraplegias, lively reflexes due to isolated parts of the transected cord, and destruction of afferent or efferent tracts. An injured brachial plexus may further complicate the picture. Traction during delivery is held responsible for most of the damage. It is deplored that obstetric writers almost ignore the subject. A good contribution.

N. Y.

MANAGEMENT OF THE SICK INFANT. By LANGLEY PORTER, B.S., M.D., M.R.C.S. (ENG.), L.C.R.P. (LOND.), Professor of Clinical Pediatrics, University of California Medical School; and WILLIAM E. CARTER, M.D., Instructor in Pediatrics, University of California Medical School, San Francisco. Third revised edition. Pp. 726; 72 illustrations. St. Louis: The C. V. Mosby Company, 1927. Price, $8.50.

A THERAPEUTICS FOR INFANCY—arranged for ready reference and characterized by explicitness. The most frequent symptoms are taken up *seriatim*, their etiology briefly discussed, and their management clearly and completely explained. Infantile diseases are next discussed under the headings of the specific infections and under the several bodily systems. A large number of diagnostic and therapeutic techniques are precisely described with the aid of excellent

photographs and drawings. Another chapter gives many formulas and recipes for infant feeding. Finally, a chapter on drugs, giving actual prescriptions useful in various clinical conditions, will be welcomed by the practitioner who treats many children.

J. S.

LECTURES ON INTERNAL MEDICINE. By KNUD FABER, M.D., Professor of Internal Medicine, University of Copenhagen, Denmark. Pp. 147; 43 illustrations. New York: Paul B. Hoeber, Inc., 1927. Price, $3.00.

THOSE, who had the pleasure to hear Doctor Faber on the occasion of his visit to the United States in 1926, will welcome the publication in book form of the four lectures delivered by him on that occasion. They are handled in the delightful philosophic style that the author so well showed in an earlier work, "Nosography." The subjects covered are "The Etiology and Pathogenesis of Achylia Gastrica," Hatfield Lecture delivered at the College of Physicians in Philadelphia, "The Intestinal Origin of Pernicious Anemia," given before the American College of Physicians at Detroit, "Benign Glycosuria," Herter Lecture at Baltimore and "Historical Outline of Medical Therapy," Harvey Lecture, before the New York Academy of Medicine.

R. K.

HOW TO MAKE THE PERIODIC HEALTH EXAMINATION. By EUGENE LYMAN FISK, M.D., Medical Director, Life Extension Institute and J. RAMSER CRAWFORD, M.D., Assistant Medical Director, Life Extension Institute. Pp. 393. New York: The Macmillan Company, 1927. Price, $4.00.

A DETAILED outline of the technique for periodic health examination, replete with tables, questionnaires, forms and charts, and leaving nothing to chance or the imagination of the examiner.

R. K.

APPLIED PHYSIOLOGY. By SAMSON WRIGHT, Middlesex Hospital, London. Pp. 418; 36 illustrations. New York: Oxford University Press, American Branch, 1926.

A LARGE amount of valuable data have been collected in this book and the relationship of physiology to clinical practice is made evident. The data are presented as facts with little discussion of the principles involved. The book is likely to be more used in preparation for examination than for the acquisition of knowledge.

H. B.

PRACTICAL LECTURES ON THE SPECIALTIES OF MEDICINE AND SURGERY. Delivered under the Auspices of The Medical Society of the County of Kings, Brooklyn, N.Y., Second Series, 1924–1926. Pp. 590; 110 illustrations. New York: Paul B. Hoeber, Inc., 1927. Price, $7.00.

FIVE years ago, The Kings County Medical Society of Brooklyn began a series of practical lectures by men of recognized ability in their own fields as a sort of postgraduate course for the members of the society. So well received were these lectures that a further experiment was attempted in 1925, in that the lectures were published in book form. The reception of this work was so satisfactory that the second, present volume, has seemed justified. Thirty-seven lectures cover the most varied fields of medical science and in a concise manner present the latest views on the subject. The work is profusely illustrated. R. K.

THE ENLARGED PROSTATE. By KENNETH M. WALKER, F.R.C.S., M.A., M.B., B.C., Jacksonian Prizeman and Hunterian Professor, Royal College of Surgeons, 1911, 1922, 1924; Lecturer in Venereal Diseases, St. Bartholomew's Hospital; Surgeon, with charge of Genitourinary Department, Royal Northern Hospital; Surgeon to St. Paul's Hospital, London, England. Pp. 190; 59 illustrations; front plate in colors. New York: Oxford University Press, American Branch, 1926.

A SHORT treatise, well rounded into thirteen chapters, dealing with the various phases of prostatic obstructions and intended for the general practitioner. There is nothing radical or dogmatic, and much that is good common sense, sound judgment and convincing argument. The final chapter, Mortality and Prognosis, is especially valuable in being an effort to present to the family physician the changed outlook for the prostatic that the past two decades have brought in refinements of treatment. Of criticism little is called for; brevity and fact pervade the work, though one cannot but regret the poor character of the illustrations. A. R.

PERNICIOUS ANEMIA. By FRANK A. EVANS, M.D. Pp. 170. Baltimore: Williams & Wilkins Co., 1926. Price, $2.50.

THE very fact that pernicious anemia still remains a morbid entity whose diagnosis may often have to be based on a careful estimate of clinical and pathological data, rather than on certain

definite signs or tests, is one that makes such a presentation as this of value. All phases of this common and interesting but perplexing disease are presented in a clear, concise and adequate manner; but one must regret the lack of an historical approach whose perspective in just such a disease affords a valuable orientation to the reader. The anemia, properly considered as only a part of the complex clinical syndrome, is properly presented from the dynamic aspect of a disturbance of the balance of blood formation and destruction—the mechanism of which is here inadequately called "hematopoietic." In the chapter on treatment most of us will not agree with the author's pessimistic views about arsenic or that iron is useless, for the reason that in hemolytic anemias the liberated iron is carefully conserved. Neither are his pessimistic views on the value of splenectomy acceptable to the reviewer at least, whose own conclusions have apparently been misconstrued by the author. Minot's recent report on dietary treatment (*J. Am. Med. Assn.*, August 14, 1926), too late to be included in the book, is too valuable not to be mentioned here. The total lack of illustrations is perhaps to be explained on grounds of economy. With few exceptions, the book is typographically correct, and can be high recommended to those wishing a more complete statement than is possible in textbooks. E. K.

HISTORY OF CARDIOLOGY. By LOUIS FAUGERES BISHOP, M.A., M.D., Sc.D., F.A.C.P., President, Medical Association of Greater City of New York; formerly Professor of Diseases of the Heart, Fordham Medical School, New York City; and JOHN NEILSON, JR., B.S., M.D., Assistant in the Cardiac Clinic, St. Luke's Hospital, New York City; introduction by VICTOR ROBINSON, M.D. Pp. 71; 12 illustrations. New York: Medical Life Press, 1927. Price, $5.00 (limited autographed edition.)

AND now the autographed edition in medical publications! Except for the added value of the two signatures and the preceptual superscription, the scant hour's reading of the thirty-nine actual pages of text hardly seems worth the price of admission. The biographic thumbnail-sketch method, covering too much and nothing well, and not even always introduced in logical sequence, fails to give either a connected view of the topic or information not easily available elsewhere. The illustrations are well chosen, but at times poorly reproduced and poorly placed. Let us hope that the author, an enthusiast on the subject, will soon produce something worthier of his skill. E. K.

BOOKS RECEIVED.

Routine Procedures. The Lankenau Hospital, Philadelphia. Edited by Edward L. Bortz, M.D. Pp. 95. Philadelphia: The Lankenau Hospital, 1927. A handy compilation of diagnostic methods, treatments, emergency measures and technique for the use and guidance of the interns in the Lankenau Hospital.

A Compend of Physiology. By Albert P. Brubaker, A.M., M.D. Sixteenth edition. Pp. 281; 27 illustrations. Philadelphia: P. Blakiston's Son & Co., 1927. (To be reviewed later.)

An Illustrated Guide to the Slit Lamp. By T. Harrison Butler. Pp. 144; 158 illustrations. New York: Oxford University Press, American Branch, 1927. Price, $9.00. (To be reviewed later.)

Dental Education in the United States. Bulletin No. 19, Carnegie Foundation for the Advancement of Teaching, 1926. Pp. 692. (To be reviewed later.)

Heart and Athletics. By Dr. Felix Deutsch and Dr. Emil Kauf. Translated by Louis M. Warfield, A.B., M.D. Pp. 187; 19 illustrations. St. Louis: C. V. Mosby Company, 1927. Price, $2.50. (To be reviewed later.)

Pioneer Medicine in Western Pennsylvania. By Theodore Diller, M.D. Pp. 230; 26 illustrations. New York: Paul B. Hoeber, Inc., 1927. Price, $3.00. (To be reviewed later.)

Directory of the American Board for Ophthalmic Examinations. Vol. I. Pp. 119.

Chemical Tests. A Manual for Chemists and Physicians. By Russell C. Erb, B.S., M.S. Pp. 262. Easton: The Chemical Publishing Company, 1927. Price, $3.00. (To be reviewed later.)

Bone Sarcoma. By Anatole Kolodny, M.D. Pp. 214; 104 illustrations. Chicago: Surgical Publishing Company, 1927. (To be reviewed later.)

Practical Otology. By Morris Levine, M.D. Pp. 387; 148 illustrations. Philadelphia: Lea & Febiger, 1927. (To be reviewed later.)

City Health Administration. By Carl E. McCombs, M.D. Pp. 524. New York: The Macmillan Company, 1927. (To be reviewed later.)

Medical Department of the United States Army in the World War. Vol. XI. Surgery. Pp. 1324; 615 illustrations. Washington: Government Printing Office, 1927. (To be reviewed later.)

Methods and Problems of Medical Education. (Seventh Series.) Pp. 99; illustrated. New York: Division of Medical Education, Rockefeller Foundation, 1927. (To be reviewed later.)

Manual of Bacteriology. By ROBERT MUIR, M.A., M.D., Sc.D., and the late JAMES RITCHIE, M.A., M.D. Eighth edition. Pp. 821; 217 illustrations. New York: Oxford University Press, American Branch, 1927. Price, $4.75. (To be reviewed later.)

The Health of the Child of School Age. By various authors, edited by SIR THOMAS OLIVER, M.A., M.D., F.R.C.P. Pp. 204. New New York: Oxford University Press, American Branch, 1927. Price, $1.80. (To be reviewed later.)

Allgemeine und experimentelle Pathologie. By DR. HERMANN PFEIFFER. Second edition. Pp. 649; 56 illustrations. Berlin: Urban and Schwarzenberg, 1927. (To be reviewed later.)

Hygiene and Sanitation. By GEORGE M. PRICE, M.D. Pp. 286. Fifth edition. Philadelphia: Lea & Febiger, 1927. Price, $2.25. (To be reviewed later.)

Progressive Medicine. June 1927, Vol. II. Edited by HOBART AMORY HARE, M.D., LL.D. Pp. 387; 69 illustrations. Philadelphia: Lea & Febiger, 1927.

Social Factors in Medical Progress. By BERNHARD J. STERN, PH.D. Pp. 136. New York: Columbia University Press, 1927. Price, $2.25. (To be reviewed later.)

Surgical Clinics of North America. Cancer Number, April, 1927. Pp. 231; 113 illustrations. Philadelphia: W. B. Saunders Company, 1927.

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Present Status of Curability of Bronchial Asthma.—It is well known that asthma and hay fever are supposed to be manifestations of allergy. This is a point of view and a theory which has afforded an excellent basis for the study of the disease. The conception that these two conditions are very closely related to allergy depends upon the fact that the sensitization or anaphylaxis may be hereditary or acquired. It is a specific phenomenon and atropin relieves the manifestations of the condition. Cooke some years ago suggested that hay fever may be entirely an idiosyncrasy, which may have nothing to do with the phenomenon of anaphylaxis. Except for one or two similar remarks and publications by other authors, the general feeling has been that there is no question that these two conditions are directly dependent upon protein sensitization to the causative ragweed or whatever other protein might be the causal factor. It has remained for KAHN (*Arch. Int. Med.*, 1927, **39**, 621) to question whether the basic cause of the condition is dependent upon anaphylaxis. He bases his opinions not only upon his own observations, but also upon the series of questions which he sent to various men interested in the subject, anaphylaxis, and those who have had considerable experience in the treatment of the condition, asthma. From a study of the answers to this questionnaire and from his own observations, he believes that asthma is not a condition primarily dependent upon protein sensitization. Protein sensitization is undoubtedly one of the outstanding phenomena of the disease, but it is a question to the author if it is the basic cause of the condition, because of the fact that desensitization or immunization is useless in an endeavor to secure an absolute cure; this is a distinct index that there is something more to the condition than simply the protein

poisoning. He believes that the final solution in discovering the genesis of bronchial asthma lies in the study of heredity and that the condition is rooted to the biological and physicochemical structure of the chromosomes.

On the Combination of Angina Pectoris and Severe Anemia.—HERRICK (*Am. Heart J.*, 1927, **2**, 351), who is responsible very largely for the increased recognition of the syndrome which was clinically unrecognized before the appearance of his classical paper, namely, the syndrome of coronary thrombosis, now calls attention to the frequent association of another interesting combination of disorders, angina pectoris and severe anemia. It will be very interesting indeed to note the response of current medical publications to these observations of the author. Will they be as generally and as promptly confirmed as were the observations on coronary thrombosis? The mechanism of the production of angina with marked anemia apparently depends upon blood of a poor quality flowing through narrowed coronary arteries with a more pronounced tendency to produce heart pain than when normal blood goes through the same arteries. This consideration assumes that the coronaries are directly concerned with the production of the pain of angina dependent upon ischemia of the myocardium. The lesson to be drawn from the paper, aside from the additional weight that is given to the hypothesis which accounts for anginal pain by relative ischemia, is that in patients with angina pectoris and with anemia, active treatment should be directed toward the correction of the latter symptom with an idea of alleviating the more severe and pronounced symptoms of stenocardia.

SURGERY

UNDER THE CHARGE OF

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An Experimental Study of the Lymphatic Theory of Pancreatitis.—KAUFMANN (*Surg., Gynec. and Obst.*, 1927, **44**, 15) says that the question of the etiology of pancreatitis has long been a source of keen interest in medicine. Starting with the work of Claude Bernard and Klebs, a great deal of evidence, experimental and clinical, has been gathered in an effort to arrive at some satisfactory explanation for the causation of the condition. There are three possible explanations. The first of these deals with the conversion of the common bile ducts and the duct of Wirsung into one continuous channel, permitting the entrance of

infected or chemically altered bile into the pancreas. The second deals with the possibility of the regurgitation of duodenal contents through the ampulla into the duct of Wirsung; while the third deals with the extension of an inflammatory lesion from neighboring organs, particularly the gall bladder and the bile ducts to the pancreas, by way of the lymphatics. The author finds that no proof has been produced that would permit us to accept the lymphatic theory on anatomic grounds. The experimental evidence in the light of his results and the consideration of the results of other investigators, fails to demonstrate a lymphatic route of infection to the pancreas. The clinical proof which has always been based on the assumption that experimentally and anatomically the lymphatic route of infection was possible, must of necessity be regarded as not existing.

Observations on Operations for Gall Bladder Disease.—FALLON (*Boston Med. and Surg. J.*, 1927, **197**, 171) claims that 90 per cent of his 1103 operations on the gall bladder and bile ducts were for gall stones. Four-fifths were women and four-fifths of these women had borne children. Mortality from 1914 to 1921 was 7.7 per cent, in 1922, 5.2 per cent, while in 1925 the mortality had fallen to 1.9 per cent. The patients were not selected, while the operation done has been, with very few exceptions, cholecystectomy. Since 90 per cent of the author's experience has been for gall stones, he has become wary in the removal of gall bladders without stones. It is often difficult both for the internist and for the operator to tell when a gall bladder, in the absence of stones, is or is not diseased. While hepatitis in greater or less degree as a rule accompanies cholecystitis, it is noteworthy that such hepatitis gives no definite clinical picture. We are as yet on the threshold of knowledge concerning disease of the gall bladder without stones and when it comes to the question of removing such a gall bladder we must depend mainly upon a thoroughly exclusive diagnosis. In our present state of knowledge it seems reasonable to infer that the cholesteremia of pregnancy is the most common cause. In taking the history of women gall stone patients it is of diagnostic value to find that frequently the first colic or pain began either in the late months of pregnancy or soon after a confinement. History still plays a very important part in diagnosis. Authorities agree that cholecystitis is the most frequent cause of so-called dyspepsia—very much more frequent as a cause than is peptic ulcer. Gall bladder dyspepsia is of the flatulent type—due not to the quantity but rather to the quality of the food taken, such as raw apples, acid fruits and greasy foods. The author's greatest lesson in twenty-five years' experience is the need of early operation, for gall stones may cause all of the diseases that may result from an ever present focus.

The Surgery of Gastric and Duodenal Ulcer.—FINNEY (*Am. J. Surg.*, 1926, **1**, 323) says that since the cause of gastric and duodenal ulcer is unknown, and since its presence is a menace to the comfort and happiness of the individual, who is constantly exposed to the greater dangers of hemorrhage and perforation, it would appear that resection of the ulcer is indicated. This is no guarantee that it might not recur. It would also appear that that form of surgical procedure which dis-

turbs least the normal physiological relationship of the stomach would be the method of choice. Beginning with these two general propositions, pyloroplasty or gastroduodenostomy, associated where possible, with resection of the ulcer would be the procedure of choice. The acceptance of these general principles would relegate to second or third choice the operation of gastroenterostomy or extensive gastric resection. Extensive resection of the stomach is reserved almost entirely for malignant disease for the author is convinced that the sacrifice of large portions of the stomach wall, interfering as it does with both motor and secretory functions of the stomach, is not justifiable as a routine procedure. More important, however, than almost anything else is the mental attitude of the surgeon in approaching an operation. It is a serious handicap to start in to operate with a fixed determination to do a certain form of operation, no matter what the conditions may prove to be. It is bad judgment and worse surgery to attempt to push any operative procedure beyond its natural limitation.

Phlegmonous Gastritis.—MEYER, BRAMS and GUY (*Surg., Gynec. and Obst.*, 1927, **44**, 361) report two cases of phlegmonous gastritis in order to emphasize the fact that this condition is not as rare as it is ordinarily supposed to be. There are several reports in the literature of cases of both the diffuse and localized varieties, in which operation was followed by recovery. The condition may be due to a bacteremia or extension from a focus elsewhere in the body or may be associated with a local pathologic condition in the stomach. The two reported cases were examples of each of the two ways in which this condition may arise. The essential pathology consists of a seropurulent infiltration chiefly of the submucosa associated with considerable round-cell involvement of this layer. The process may be localized or diffuse, involving the entire stomach, but ending abruptly at the esophageal and pyloric orifice. The gross appearance is that of a very much thickened stomach wall, which is very boggy, exudes pus from the cut section and in which the mucosa is usually intact. The clinical picture combines the features of the so-called acute surgical abdomen, with the phenomena of generalized sepsis.

Present-day Status of the Surgery of Brain Tumors.—SACHS (*South Med. J.*, 1927, **20**, 171) states that fifteen years ago a craniotomy for brain tumor had a mortality of at least 80 per cent. It was unusual for a tumor to be found at operation and still rarer for it to be removed. The most frequent operative procedure was a decompression operation to save the patient's eyesight and frequently it was inadequately done, so that it did not even accomplish this, for the underlying principles of the decompression operation were not well understood. The most favorable type of tumor in the brain is an encapsulated tumor and these in the brain are the endotheliomas. They grow slowly, often over a period of years and may become very large, and for this reason their removal may offer great technical difficulties, but when they are removed a permanent cure results. Another type of case that has an excellent prognosis and in which we have permanent cures is the gliomatous cyst. In these cases the symptoms are very different from those in the endotheliomas, for these patients have the general symp-

toms of increased intracranial pressure, headache, vomiting and failing vision. The author believes that the rate of growth of the gliomatous cyst and the fact of whether the circulation of cerebrospinal fluid has been interfered with are two factors of importance in symptomatology. The third group of tumors is the solid gliomas. These constitute about 35 to 45 per cent of all brain tumors. It is this group that presents the greatest problems. It is the results with many of this group that discourage the neurologist and general practitioner so much. The question arises, Can infiltrating tumors be removed, and how grave is the danger? Radical resection and palliative decompressions are the methods of attacks. There is also the class of benign papillomas or angiomas. There is also the destructive acoustic neuromas—a group of tumors of the eighth nerve. These tumors grow very slowly and are dealt with by partial intracapsular enucleation.

Hyperpiesis.—BARTON (*West London Med. J.*, 1927, **32**, 14) claims that the modern clinical units combined may soon clear up this great want of progress in the diagnosis of the disease which causes hyperpiesis (high blood-pressure states). The section of urology will contribute the chief work. Fundamental subjects must be gone over. The biochemist and therapeutist may then come on the scene. The author would prophesy that the surgeons will imitate what they have done in taking other diseases within the abdomen under their hands—alluding to the modern treatment of gastric ulcer, duodenal ulcer, the gall bladder and its numerous affections. The spleen is frequently removed by them with success in diseases which were thought to be purely medical. Apart from the purely surgical diseases of the kidneys, the surgeons have already made several bold attempts for this field to come under their ken. Reginald Harrison proposed decapsulation of the kidneys in acute parenchymatous nephritis. Sir Arbuthnot Lane proposed to remove all colons in intestinal stasis in which condition the bacteriologists held that streptococci were the chief cause of all hyperpiesis.

Successful Operation in Eight Cases of Pulsion Diverticula of the Esophagus.—LAHEY (*Boston Med. and Surg. J.*, 1927, **196**, 343) claims that removal of pulsion diverticula of the esophagus, when done in two stages and under local anesthesia, is remarkably safe. Pulsion diverticula occur at the point where the esophagus begins on the posterior wall in the midline, just below the last transverse fibers of the inferior constrictor muscle and within the little triangle bounded on either side by the oblique fibers of the cricopharyngei and above by the transverse fibers of the inferior constrictor. The point has been called the pharyngeal dimple, owing to the fact that the esophagus is not protected by muscle here. In each of the eight cases in which the author has operated the body of the sac of the diverticulum was found to have descended and lay to the left of the esophageal tube. When the one-stage procedure was employed in removing the diverticula mortality was high because of the frequency of leakage in the suture of the esophagus following immediate amputation of the sac, and the secondary and frequently fatal cellulitis and mediastinitis. But with the two-stage procedure, the sac being first implanted unopened in the wound and later removed (nine to ten days later), this main cause of death has been eliminated.

Reconstruction of the Anterior Crucial and Internal Lateral Ligaments of the Knee Joint.—HORAN (*Brit. J. Surg.*, 1927, **14**, 569) says that reconstruction of the anterior crucial and internal lateral ligaments of the knee joint from fascia lata has been performed in a series of 11 cases of tearing or stretching of these ligaments. Examination of the results of the operation after periods varying from one to six years has been possible in 10 of these. The operation results in a joint capable of withstanding the stress and strain to which it is subjected in the course of ordinary and average life. Early and thorough reëducation of the musculature of the limb is important to success. Prolonged immobilization of the joint by splinting or plaster following operation is to be avoided, as is the mechanical support of the joint at a later period by a knee cage or similar appliance with the inevitable atrophy and impaired support of the musculature governing the joint.

THERAPEUTICS

UNDER THE CHARGE OF

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Synthalin—Substitute for Insulin for Oral Medication.—FRANK, NOTHMANN and WAGNER (*Klin. Wchnschr.*, 1926, No. 45, p. 2100) report a synthesized product, called synthalin, which is an alkaline guanidin derivative. It lowers blood sugar and can be taken by mouth. When given to rabbits which have been starved twenty-four hours, in doses of 3 to 4 mg. per kilo, it reduces the blood sugar to the point of convulsions. These are immediately relieved by the injection of glucose. In depancreatized dogs synthalin given in sufficient quantities causes a cessation of the glycosuria and lowers the blood sugar to the borderland of convulsions. In human diabetics it may cause the disappearance of 30 to 40 gm. of glucose from the daily output of urine. Its action is more delayed than that of insulin, being retarded sometimes as long as twenty-four hours, but it continues over a longer period of time. It may produce, even in therapeutic dosage, a loss of appetite, rapid peristalsis, nausea and possibly vomiting. The authors recommend, therefore, commencing with small doses and working gradually up to what is necessary. When it is desired to change from the insulin treatment to the newer synthalin it is recommended also that both drugs be given at the same time, and that the amounts of synthalin be slowly increased while at the same time one lowers the dosage of insulin correspondingly. They conclude that this preparation lowers the sugar in the urine, 1 mg. of synthalin taking care of 1.1 to 1.2 gm. of sugar; that the blood sugar is brought down below the point where glycosuria

occurs; that acidosis is relieved; that other symptoms of diabetes, such as polyuria and polydipsia, are removed. It is found useful in cases with temporary infection or those that are "insulin refractory;" in diabetics with surgical infections, such as gangrene, furunculosis and phlegmons, it may be used in place of insulin. The contraindications for the use of synthalin are severe acidosis and diabetic coma, when the more powerful and more rapid action of insulin should be depended on until the emergency is past.

PEDIATRICS

UNDER THE CHARGE OF

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Malabsorption in Deficiency Diseases.—BURNETT and HOWE (*J. Am. Med. Assn.*, 1927, **88**, 1705) point out that deficiency disease is a term applied to maladies that are caused by the lack of one of the accessory food factors, but they feel that this application is too limited. The supposedly specific nature of the vitamins is responsible for this point of view, for while incomplete food will ultimately bring about easily recognized terminal lesions, the early metabolic disorders of intestinal indigestion, malabsorption, and constipation or diarrhea have not been generally observed. The oversight is due to a failure to understand and apply indexes of normal absorption. There is a normal form of the feces and a normal intestinal rate and these should serve as a valuable sign in early and slight deviations of health. An understanding of the restricted limits of normal absorption leads to the recognition of two subtle and vaguely symptomatic types of malabsorption. In one, through a lack of appetite, insufficient food is ingested, and there is an abnormal retention of the intestinal contents. Dejections are infrequent and scanty. In the other, enough food is consumed but because it is incomplete or faulty it passes too rapidly through the digestive tract. In both types the metabolic disorder is due to the ailment and not to the nutritive apparatus. Both types of malabsorption have been recorded by investigators of the human deficiency diseases of rickets, beriberi, scurvy and pellagra. If the restricted limits of normal absorption are applied to the metabolic diseases, the faulty food factors of eating too fast and too much, too little food, badly proportioned diets or habitually using physic or enemas act somewhat like food without the accessory substances, in producing indigestion and malabsorption. By the recognition of a normal form of the feces, a normal intestinal rate and a normal body weight, early and slight functional disorders of anabolism can be observed and treated, and an improved state of well-being can be maintained. Without applying these indexes of normal absorption, the failure in the

transfer of nutrient molecules to the body may continue for years before the factors of safety in the weakest tissue are exhausted and the readily recognized and destructive changes of a deficiency disease are apparent.

Bone Changes in Renal and Celiac Infantilism.—PARSONS (*Arch. Dis. Child., London*, 1927, **2**, 1) presents the clinical characteristics and the chemical and Roentgen ray observations in 5 cases of renal infantilism with bone changes. He attempts to classify the bone changes and to explain their pathogenesis. He submits evidence that the bone deformities are rachitic in nature, but he has not been able to produce curative effects in renal rickets by ultraviolet irradiation, whereas in celiac rickets such treatment results in cure. The explanation of these results is probably to be found in the fact that the ultraviolet rays raise the blood phosphorus by increasing phosphorus absorption, and therefore treatment by this method makes the disparity between the calcium and the phosphorus more marked. The author thinks that this makes the disease much worse. The factors necessary for the prevention of rickets are usually stated to be an adequate supply of calcium, phosphorus and vitamin D in the diet. Renal rickets develops and persists in spite of an adequate supply of all of these factors and hence the suggestion of Shipley that under certain circumstances rickets may have an endogenous origin appears to have foundation. The bone deformities of renal rickets are those of true low calcium rickets. The Roentgen ray shows that the case of renal rickets may develop bone changes of one of three types: Atrophic rickets; florid rickets or wooly rickets. The primary cause of renal rickets is the inability of the kidney properly to excrete phosphates. In these cases a true endogenous rickets exists. The blood shows marked lipemia, nitrogenous and phosphate retention and an acidosis. Blood calcium while low compared with blood phosphorus, frequently shows normal values, in contradistinction to what usually obtains in azotemic nephritis and after the injection of phosphate. The suggestion is made that this is due to mobilization of the calcium from the bones as a preventive mechanism against tetany. Healing of rickets may occur in those periods in which phosphorus excretion improves materially, or when the growth period is over.

The Production, Collection and Distribution of Human Milk.—HOOBLER (*J. Am. Med. Assn.*, 1927, **88**, 1786) from ten years of experience feels that an almost unlimited amount of human milk can be secured. In their clinic they are not availing themselves of the total output of the mothers. After studying the output of many mothers who are quantity producers by nature, he has found that there are also mothers who are minimum producers by nature. For every mother who produces less than enough to nourish her infant properly there is another mother who produces enough to supply her own child amply as well as to give some toward supplying the deficiency of other mothers. There is a potential supply if evenly distributed would supply all children with human milk, which is the natural food. Hoobler feels that if every child during its first month of life could be fed on wholesome breast milk, the death rate during this precarious first month would be greatly

reduced, and the morbidity of the following months of the dangerous first year would be greatly diminished. Bureaus have been established in at least twenty centers of population across the country. Every large city should in its maternity hospital maintain a station for the collection and distribution of human milk. Points as far away as twelve hours can be served from such a collection depot. Human milk has been dried and fed with good results. This suggests a suitable disposition of excess quantities. By using a drier apparatus a dried supply can be kept on hand for emergency use and the dried product can be shipped over larger areas.

Pasteurized Milk as Food for the Infant.—LEVINE (*Arch. Ped.*, 1927 **44**, 273) reminds us that when artificial feeding is resorted to, the infant is compelled in most instances to subsist on one food and that is pasteurized milk. The obvious deficiencies of pasteurized milk in vitamin C are supplemented by orange juice. There may be deficiencies that are as yet unrecognized. In view of recent findings with reference to the pathologic effect of dead bacteria or sterile bacterial filtrates and with reference to the profound deterioration resulting from the application of heat, it is very imperative to reëvaluate the nutritive value of milk not merely on the basis of its freedom from living microorganisms, but on the basis of its ultimate effect on the growth of the patient and the maintenance of a state of health. In pasteurizing milk there has been found a safety in one direction by a method which will show decided harm in other directions. The greater morbidity and the greater mortality among infants artificially fed renders investigations along these lines an urgent necessity.

The Vital Capacity of the Negro Child.—ROBERTS and CRABTREE (*J. Am. Med. Assn.*, 1927, **88**, 1950) undertook this study in order to ascertain the vital capacity of a group of normal negro children and to compare these vital capacities with those of a group of white children living in the same area. Because the negro children are heavier than white children of the same age and height, and because in many other ways the standards differ, it was thought advisable to undertake this investigation. The results are based upon observations on 1564 white children and 1254 negro children. These children are both from urban and rural communities and form more than 25 per cent of the total school population of the county. The negro children were found to have vital capacities lower than white children of the same age. The difference is greater in the case of the boys. White girls exceeded negro girls by 7.2 per cent, and white boys exceeded negro boys by 12 per cent in the vital capacity. Negro children have vital capacities lower than white children of the same body weight. The white girls exceeded the colored girls by 10.2 per cent and the white boys exceeded the negro boys by 14.9 per cent in vital capacity. Negro children have vital capacities lower than white children of the same standing height. The white girls show vital capacities averaging 6.8 per cent higher than negro girls and the white boys have vital capacities that average 11.2 per cent higher than those of negro boys. Negro children have the same vital capacities as white children of the same stem length.

Endemic Meningococcus Meningitis.—CAFFEY, MCLEAN and SULLIVAN (*J. Am. Med. Assn.*, 1927, **88**, 1859) found that in purulent meningitis before treatment, the sugar concentration of the cerebrospinal fluid was markedly decreased in 90 per cent of the cases. A small number of the cases showed normal sugar concentration. The administration of specific serum in children older than six months who recovered caused an increase in the cerebrospinal-fluid sugar to normal within from seventy-six to ninety-six hours. The administration of specific serum in patients younger than six months who recovered caused a slower increase in cerebrospinal-fluid sugar. Normal values were not reached during two weeks after the beginning of the treatment. The administration of specific serum in uncomplicated fatal cases did not cause a material increase in cerebrospinal-fluid sugar. The cerebrospinal-fluid chlorid content was reduced in 60 per cent of the cases before treatment. In cases in which the chlorids were decreased, the administration of serum caused an increase to normal in cases in which there was recovery. Increase of cerebrospinal-fluid sugar is therefore a favorable prognostic sign. Failure of cerebrospinal-fluid sugar to increase during serum therapy in patients older than six months is an unfavorable prognostic sign, but failure to increase in children under six months of age is not necessarily an unfavorable sign. As regards the quantitative determinations of cerebrospinal-fluid chlorids these are not of much value in diagnosis or prognosis.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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Basal Metabolism in Ichthyosis.—Clinically it has been observed that the dry, scaly and harsh condition of the skin in ichthyosis closely resembled that found in myxedema and cretinism, which are definitely known to depend on hypothyroidism although there are cutaneous histopathological differences. In many cases of severe ichthyosis some abnormality of the thyroid gland has been described when careful postmortem examinations have been performed. The relationship between ichthyosis and the activity of the thyroid gland has been obscure until the advent of the modern methods of estimating the basal metabolic rate. Using Haldane's gas analysis apparatus and Du Bois' formula and chart, PORTER (*Brit. J. Dermat. and Syph.*, 1926, **38**, 475) estimated

very carefully the basal metabolic rate of 10 ichthyotic children and 7 adults who had mild cases of ichthyosis, all developing after puberty. In 70 per cent of the children and 25 per cent of the adults, the rate was found to be subnormal; it was as low as −33 in several children. However, the lowness of the rate did not always correspond to the severity of the case. As the thyroid normally becomes more active at puberty, it is only to be expected that any existing hypothyroidism would be partially compensated for after adolescence had been attained. In six clinically normal mothers of ichthyotic children 66.6 per cent were found to have increased basal metabolic rates and only 16.6 per cent a decreased rate. The hyperthyroidism in the mothers is difficult to explain on theoretical grounds. Eight out of the 12 ichthyotic cases treated with thyroid extract improved under treatment; and, of these 8, the rate was below normal in 7 and normal in 1. No case with the rate above normal showed definite improvement; those having the lowest rates showed the greatest improvement. The author believes these observations to point to hypothyroidism as the main factor in the production of ichthyosis.

OBSTETRICS

UNDER THE CHARGE OF

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Antepartum Hemorrhage Due to Separation of a Normally Implanted Placenta.—Lull (*Atlantic Med. J.*, 1927, **30**, 570) performed Cesarean section 3 times within six weeks for antepartum hemorrhage caused by the separation of a normally implanted placenta. Hysterectomy was done in 1 case; all 3 patients recovered. The operation is best performed under a general anesthetic, as rapidly as possible, with removal of the uterus if there is any hemorrhage of the uterine musculature, as there is a tendency in these cases for the uteri to relax and cause postpartum hemorrhage. The condition was formerly thought due to traumatism, but has been very definitely proved that these patients form a type of toxemia which is the basic etiologic factor.

A Case of Eclampsia with Relatively Low Blood Pressure.—Desser (*Am. J. Obst. and Gynec.*, 1927, **13**, 647) reports a case of eclampsia with coma and convulsions in a primipara, aged twenty-seven years, with a blood pressure averaging 120 systolic and 80 dystolic, with uneventful recovery following induction of labor in the thirty-fifth week of pregnancy.

Virginia's Sterilization Law Valid.—The authority of the state of Virginia (*Atlantic Med. J.*, 1927, **30**) to order sterilization of mental defects was upheld by the United States Supreme Court in an opinion handed down by Associate Justice Holmes for the majority of the Court. The contested case was a feeble-minded white woman committed to the State Colony for Epileptics and Feeble-minded, the mother of an illegitimate feeble-minded child, upon whom the Circuit Court ordered the operation of salpingectomy performed under the Virginia State Law.

A Case of Intraäbdominal Pregnancy, with Living Child.—A full-term intraäbdominal pregnancy with subsequent delivery of a living child came under the care of DALY (*Am. J. Obst. and Gynec.*, 1927, **13**, 649). A tentative diagnosis was made in the sixth month of pregnancy, but operation was refused until eclampsia occurred in the eighth month. Operation resulted in a living child found under the liver on the right side. The uterus showed a small rupture in the fundus with a cord protruding through the opening, the placenta itself being found in the uterine cavity. The mother died, thoroughly toxic and shocked.

Rectal Analgesia in Obstetrics.—Further studies in the effect of the Gwathmey method of producing analgesia during labor by the use of morphin-magnesium sulphate, given hypodermatically, combined with the rectal instillation of an ether-oil combination, were made by MCNIELE and VRUWINK (*California and Western Med.*, 1927, **26**, 640), who believed a rigid adherence to the technique is essential. In 700 patients (over half of whom were private patients) some relief was secured in 90 per cent and marked relief in 75 per cent. The method is applicable in the home and is safe for mother and child. They have modified the original Gwathmey technique, with, as they believe, more satisfactory results. In 200 cases the hypodermics of 50 per cent magnesium sulphate without morphin were omitted with no difference in the results obtained, but the results are better when the magnesium sulphate is given with the morphin. The use of pantopon, $\frac{1}{3}$ gr., with scopolamin, $\frac{1}{200}$ gr., had no advantage as a substitution for the morphin-magnesium sulphate. The substitution of diallybarbituric acid in 3-gr. doses for the morphin-magnesium sulphate, hypodermatically, gave more pronounced rest and relaxation to the patients, increased the strength and decreased the interval of uterine contractions and gave almost immediate relaxation of the cervix and very rapid dilatation, particularly noticeable in those patients with marked rigidity of the cervix so often found in elderly primiparæ. They plan on adopting it for their outpatient service.

Pregnancy and Heart Disease.—Since 1919 pregnant women with cardiac disease, in care of the Sloane Hospital for Women, have been assigned to a special cardiac clinic under medical as well as obstetric supervision, CORWIN, HERRICK, VALENTINE and WILSON (*Am. J. Obst. and Gynec.*, 1927, **13**, 617) have studied 103 cases in one series, with 5.8 per cent mortality, and 93 others, with 6.4 per cent mortality. The average pregnant cardiac was carried along to viability or term. If circulatory breakdown occurred before the fourth month abortion

was usually considered wise; if not until later, it was usually possible to carry on suitable response to medical treatment. They noticed an increased incidence of toxemia of pregnancy in examples of cardiac disease. A relatively short duration of the second stage, the small average weight of the child and the high incidence of prematurity were noted and believed a protection to these cases.

The Advantages of Rectal Palpation during Pregnancy and Labor.—STUCKERT (*Am. J. Obst. and Gynec.*, 1927, **13**, 642) suggests, as a precautionary measure in preventing puerperal sepsis, rectal palpation should be done during the last few weeks of pregnancy and during labor. This prevents carrying germs from the lower to the upper vaginal tract, is more readily accomplished, less painful to the patient, lessens the likelihood of premature rupture of membranes and prevents traumatism to the cervix and the temptation to assist in dilatation of the cervix. The technique is simple, there are no ill effects and the examination in 90 per cent of cases in conjunction with abdominal palpation will reveal all necessary information.

An Analysis of the Results of One Hundred and Thirty Pregnancies Subsequent to Cesarean Section in Ninety-six Patients.—RICE (*Am. J. Obst. and Gynec.*, 1927, **13**, 591) studied the subsequent pregnancies in 96 cases of primary Cesarean section. He believes that in every case where proper apposition of the uterine muscle is obtained, and no infection follows, the resultant scar is replaced by normal muscle tissue, the structure and function of the uterus is not impaired and there should be no fear of rupture from overdistention during future pregnancies or labor. Infection is the most frequent cause of an imperfect scar. A faulty scar may result from improper suturing. In 96 patients there were 133 subsequent pregnancies; 76 required repeated section in 92 deliveries. Two patients were delivered by spontaneous premature labor, 7 by miscarriage and 2 by induced abortion; 13 of the 76 patients had 2 repeated sections and 1 patient three. Twenty patients delivered vaginally; of these 4 had two deliveries and 1 six deliveries; a total of thirty deliveries. When repeated section is decided upon as the method of delivery it was always performed before the end of pregnancy.

The Morbidity and Mortality of Cesarean Section.—MONTGOMERY (*Am. J. Obst. and Gynec.*, 1927, **13**, 610) finds the present-day maternal mortality rate for Cesarean section is from 2 to 3 per cent when the operation is performed under favorable conditions as an elective operation or very early in labor. DeLee reports a maternal mortality of 0.76 per cent in 390 low or cervical Cesarean sections. In reviewing a series of 25 Cesarean sections performed by various operators, all of the classical type, in the wards of the Jefferson Hospital, from September 1925, to September, 1926, there were 4 maternal deaths, 16 per cent; there were 2 deaths from sepsis, 1 from peritonitis and 1 with violent hemorrhage from placenta previa. Twenty-six infants were delivered; of these 3 were born dead, 11.9 per cent, and 3 died after delivery, 11.9 per cent; a total infant mortality of 23.8 per cent.

Pulmonary Embolism Complicating Pregnancy, Labor and the Puerperium.—Pulmonary embolism, though uncommon, must be considered one of the most serious complications of pregnancy and parturition. BUNZEL (*Am. J. Obst. and Gynec.*, 1927, **13**, 584) states that 32 cases occurred in 31,716 pregnant patients, an incidence of 0.1 per cent. More than 65 per cent of these, or 21 cases, died. The origin of the embolus is believed to be in a thrombus, occurring probably in the femoral vein, although air emboli also do occur. In the series of 32 cases pulmonary embolism occurred 6 times in the early months of pregnancy, all of which were abdominally operated upon with 4 deaths. The remaining cases occurred in the eighth or ninth month of pregnancy. Age did not appear to be a factor; these cases ranged from eighteen to forty-six years of age; none of these cases had a long first or second stage of labor. Six cases delivered normally, 7 by forceps (1 low and 6 medium), 7 by abdominal Cesarean section, 2 by breech and 2 by version and breech. In 2 of these operative deliveries Voorhees bags were employed, while in the other cases a Mannel curettage, a median episiotomy and tamponade of the uterus were done at once. Thus, the incidence of pulmonary embolism in operative deliveries is three times greater than in normal spontaneous deliveries. Of the 24 cases delivered, 16, or 66.6 per cent, died—an argument against operative interference, except when such interference is absolutely necessary. The incidence of pulmonary embolism in abdominal Cesarean section was 1.5 per cent and in cases of placenta previa 1.9 per cent. These cases show more hemorrhage than in other deliveries, and we may assume that excessive bleeding is a predisposing cause of pulmonary embolism; in the entire series of 36 cases signs of phlebitis were recorded in only 4 patients. In treatment little may be done other than the use of sedatives and cardiac stimulants.

GYNECOLOGY

UNDER THE CHARGE OF

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Artificial Vagina.—Although the Baldwin operation for the formation of an artificial vagina is well known and generally accepted by the profession, there are very few gynecologists who have had the opportunity of performing this operation often, if at all. Therefore, the report of 6 personal cases by JUDIN (*Surg., Gynec. and Obst.*, 1927, **44**, 530), of Russia, with no mortality is of interest. In all 6 cases a good artificial vagina was made, which fully satisfied both husband and wife. Some of the patients stated that they had libido and orgasm to a con-

siderable degree. There were often pains from peristalsis of the resected intestine together with an annoying secretion of mucus from the new vagina. The pain is brought on by the straining of the mesentery during increased peristalsis and its severity depends upon the width of the mesentery. These pains cannot be avoided, as it is difficult to do anything to make the mesentery longer without endangering the nourishment of the intestine, but the pains soon pass away as the intestine and mesentery adapt themselves to the new position. The abundant secretion of mucus from the intestinal loop must be counted on as an argument against the operation, but this disadvantage does not outweight the advantages of the operation, and it can probably be greatly overcome by not taking too long a loop of bowel. In addition to these 6 cases of his own, the author reports 15 other cases of Moscow surgeons which had previously been unpublished. The combined mortality of the 21 cases was less than 10 per cent.

Endometrial Implants in the Abdominal Wall.—PRATT (*J. Michigan State Med. Soc.*, 1927, **26**, 82) has investigated the interesting subject of endometrial implants in the abdominal wall, that is, in a laparotomy scar, and has found that they are not of uncommon occurrence. In reviewing 42 cases in the literature to which he has added 4 new cases, he found that it usually follows an operation in which normal endometrium has been traumatized. Ventral fixation is the most common type of operation preceding scar implantation. Special care should be taken during this operation not to penetrate the endometrium. Although the growth in the scar is seldom encapsulated, local excision seems to be sufficient for its eradication. Two cases recurred after incomplete removal, but a second operation relieved both of these. All local symptoms have been relieved by removal of the growth. Regardless of the cause of other endometrial growths, the author feels sure that this group in a laparotomy scar are due to implantation. I have personally seen 1 case of this type which entirely cleared up after local excision.

Backache.—From the standpoint of the gynecologist, sacrolumbar backache is a prominent symptom in approximately 50 per cent of all gynecologic cases, according to WARD (*Am. J Surg.*, 1927, **2**, 257). In his experience 85 per cent of the cases of backache are of gynecologic origin, while 15 per cent are orthopedic or nonsurgical. In the cases due to gynecologic disease, pelvic congestion, however produced, is a predominating factor. Traction on the pelvic visceral supports, the result of injuries incident to parturition, is a common cause, while pressure on the pelvic ganglia and nerves produced by neoplasms or exudates may result in reflex backache. In view of the considerable number of gynecologic cases seeking relief for backache, in which the symptom may be caused by factors other than pelvic disease, or which may be associated with it, the coöperation of the orthopedist, the internist, the urologist and the neurologist may be necessary for a a differential diagnosis and cure. In reviewing the records of the Women's Hospital in New York City for nine years, ending October,

1924, he found that nearly 15 per cent of the operations performed were for the correction of uterine retrodisplacements. A follow-up study of over 500 of these cases over a period of a year or longer shows that the percentage of success in the relief of the classical symptoms including backache for which they sought aid was 88 per cent. To anyone who has carefully followed his operative cases complaining of backache, this percentage of cure will seem to be unusually good, but no doubt we can all attain the same results if we select our cases carefully as the author has done, and refuse operation to those patients in whom the backache cannot be definitely attributed to the pelvic disease.

Gye's Cancer Theory.—Working in the Department of Bacteriology and Immunology of Harvard Medical School, MUELLER (*J. Exp. Med.*, 1927, **45**, 243) conducted an interesting series of experiments to determine the correctness of Gye's theory that cancer is due to a filtrable virus in combination with another substance which he termed the "specific factor." In a large series of experiments extending over a period of twelve months he found absolutely no indication of the necessity of two factors in the production of the Rous sarcoma. In other words, he has been unable to duplicate the results of Gye. The author has shown that uncontrollable local and individual variations may produce results in occasional chicks which simulate satisfactory experiments, but when viewed as a whole mean nothing. Because of the conflicting nature of results obtained by those who have undertaken to repeat the work, and on account of the difficulty of controlling all factors involved, he does not feel that it may be definitely stated that Gye's theory of the cause of cancer is wrong. On the other hand, he believes that the theory apparently needs more evidence in its support if it is to receive further serious consideration.

Ephedrin in Dysmenorrhea.—Although the Chinese have used the drug *ma huang* for many centuries with very satisfactory results, it is only within a comparatively few years that the rest of the world has been using its alkaloid ephedrin. In the past few years considerable research and clinical trial has been made with this drug, and it is found to possess results very similar to epinephrin, being quite potent when given by mouth. Inasmuch as epinephrin has been found to be of some value in cases of dysmenorrhea, which are due to disturbances of the sympathetic nervous system, it occurred to LANG (*Zentralbl. f. Gynäk.*, 1927, **51**, 1043) to try the use of ephedrin in cases of this type. He has found it quite efficient in not only relieving the pain, but also in reducing the amount and duration of the flow. He gives the drug as soon as the pain appears, giving from $\frac{1}{4}$ to 1 tablet (each tablet is 0.05 gm.), two to three times a day. The smaller dosage should always be used first and then later increased if it causes no untoward symptoms, such as cardiac palpitation. If this proves to be of as much value as he states, it will be a real addition to our therapeutic measures as epinephrin requires repeated hypodermic injections, which have always been more or less against its use.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

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Otosclerosis Associated with Blue Sclerotics and Osteogenesis Imperfecta.—CLEMINSON (*J. Laryngol. and Otol.*, 1927, **42**, 168) reported the clinical data of a female, aged twenty-three years, who exhibited the triad, otosclerosis, blue sclerotics and osteogenesis imperfecta. Although a hereditary influence is encountered in many of these cases, there was no history of similar instances in this patient's family. While it is not uncommon to find persons with any two of the three manifestations of this complex, it is more unusual to see all three in the same individual. The fragilitas ossium may be present at birth or it may develop later in life, presumably the result of a want of quantity or quality of the fibrous tissue forming the framework of various regions of the body. In other words, there seems to be a disturbance in the development of the mesenchyme. While the association of otosclerosis with defects of the mesenchymatous structures appears to be of great importance, apparently other factors, such as infection, toxins and a weakening of nerve influence, play a rôle in the inauguration of the stapedial fixation. The author presents the histopathologic picture of a case of otosclerosis, with blue sclerotics and fragilitas ossium, from Nager's Clinic.

Diphtheria Infection of the Middle Ear and Mastoid.—COSTEN (*Arch. Otolaryngol.*, 1927, **5**, 119) reported 2 cases in which the patients, aged three and a half years and thirteen months respectively, carried virulent diphtheria bacilli in their middle ears and mastoids without clinical signs referable to the ears, and exhibited obscure but persistent general reactions. In both cases the complete solution of the infantile mastoid structure and replacement with organized pyogenic membrane indicated an infection of long standing. The organisms in both cases were fatal to guinea-pigs. After the administration of antitoxin the bacilli became nonvirulent and the mastoid wounds healed. The author accounts for the conviction that aural diphtheria is rare by its atypical symptomatology and the fact that routine cultures are not subjected to special media unless requested by the surgeon. He points out that the extent of destruction in the middle ear and mastoid is much greater than the severity of symptoms would indicate.

Lymphoid Tumors of the Tonsil.—In presenting the pathologic data of four lymphoid tumors of the tonsil—one multiple and three single polypi—PEARLMAN and PILOT (*Arch. Otolaryngol.*, 1927, **5**, 143) call attention to the fact that the great majority of new growths originating from the tonsils are malignant. Of the benign tonsillar tumors, which are comparatively rare, fibromata and papillomata are the commonest, and pure lymphoid neoplasms are among the rarest varieties. No

clinical records were available in the 4 cases reported. After a résumé of the instances of lymphoid tonsillar tumors in the literature, and a description of the four cases they have encountered, the authors conclude that in their cases the outstanding histologic picture was the occurrence of hyperplastic or diffuse lymphoid tissue similar to the lymphoid tissue of the tonsil itself. They believe that, in all likelihood, their cases represent an unusual formation of hyperplastic lymphoid tissue rather than true new growths of the tonsil.

The Physics of Sinus Drainage.—Despite wide variations and disagreements in their ideas of what constitutes proper and effective suppurative paranasal sinusitis, all investigators are united as to the important rôle which drainage plays in these cases. Obscure as may be the physiologic and biochemical reactions which affect this process, PROETZ (*Ann. Otol., Rhinol and Laryngol.*, 1927, **36**, 23) calls attention to the fact that certain elementary laws of physics determine the effectiveness of the treatment and the course of the disease. From a mechanical standpoint, each sinus is a rigid-walled polyhedral air cavity which communicates with the outer air through a relatively small aperture. The passing of fluid from such a cavity depends upon such elemental phenomena as viscosity of fluids, surface tension, pressure of gases, osmosis and heat. The effects of these are modified by such biologic activities as exudation and ciliary action. Depending upon the particular sinus in question, the ostia through which these rigid chambers must drain occur in one of three positions: At the bottom, as in the frontal sinuses; at the side, as in the ethmoids and sphenoids; at the top, as in the antra. In consequence of this anatomic position of their ostia, these three types present three mechanical problems, in that they do not respond alike to physical agents, such as externally applied irrigation and suction. Normally the ostia are patent, permitting the free diffusion of fluids, but they may be entirely or partially occluded in various ways, although they may still yield to pressure from within and without. When the sinus openings are occluded positive and negative pressures may be maintained in the sinuses for relatively short periods. These tend to become rapidly equalized, however, by the absorption of the enclosed air or by exudation. To remove a fluid by suction or by postural drainage from a rigid chamber through a small opening, its viscosity must be relatively low, and it must completely cover the opening. After a detailed discussion of the viscosity of the contents of the sinuses under varying conditions, the author remarks that if their surface tension is so high, and their consistency so elastic, they may finally emerge from the sinus in a globular mass which retains its contour in the nose. The secretion within the sinuses and the determination of the fluidity of their contents, depends upon the osmosis of colloids. The author believes that, as colloidal systems are particularly sensitive to electrolytes in solution, it should be of advantage to inquire more closely into the action of salts in various concentrations with a view of improving the conditions of drainage. Inasmuch as the fluidity of the cell contents is perhaps the most important single factor in drainage, assuming that the ostium is open or can be opened, the writer lately devised and described (*Arch. Otolaryngol.*, 1926, **4**, 1) a method of irrigation by displacement of the air in the sinus cavities and the introduction of fluids

in order to thin the secretions, thus allowing them to flow out, rather than attempting to draw them out when they are too viscous to flow.

Coagulation Time Prior to Tonsillectomy.—Seeking data relative to the value of coagulation time before tonsillectomy with reference to postoperative hemorrhage, the legal value of coagulation time, the number of hospitals doing routine estimations of coagulation time and the various methods employed, HUNT (*Ann. Otol., Rhinol. and Laryngol.*, 1927, **36**, 187) sent a questionnaire to each of 567 hospitals throughout the United States and received replies from 300 of them. An analysis of the returned questionnaires showed that 68 per cent considered a routine coagulation time advisable and over a half of them (58 per cent) did a routine determination, which was usually the capillary pipette method. He says that coagulation time is not always indicative of bleeding time, and *vice versa;* that, while a routine coagulation time is desirable to complete the clinical records in a given case, it is not necessary for the welfare of the patient if a proper history has been taken; that all doubtful cases should have both coagulation and bleeding time tests. His inquiries have revealed that there is apparently no great legal risk for those who do not follow this practice, inasmuch as hemophilia is a rare disease, affecting only males and transmitted by females. The author concludes by saying that "The only apparent advantage of a routine coagulation time prior to tonsillectomy in an institution which has facilities for a thorough history and physical record is for that added margin of safety when trouble comes."

The Diagnosis of Sinus Thrombosis: A New Procedure.—"If in simultaneous blood cultures taken from the two internal jugular veins a larger number of bacteria were found in the plates made from one side than in those made from the other side, it might be inferred that the bacteria in the blood were coming from that side. One might expect such a procedure to be valuable, not only in confirming a diagnosis of thrombosis of the lateral sinus but also in determining the side involved." OTTENBERG (*Arch. Otolaryngol.*, 1927, **5**, 43) describes the technique of aspiration of the blood from the internal jugular vein and reported a case of left lateral thrombophlebitis, in a boy, aged seven years, in which the blood cultures showed more colonies of hemolytic streptococci on the right side than on the left. This, the author seeks to explain by assuming that the microörganisms may have been growing in preponderating numbers or exclusively in the upper end of the thrombus, or approximately equal numbers of bacteria may have been growing at both ends of the thrombus. He regards the latter explanation as the more plausible one. From his observations on 12 cases he has decided that bouillon flasks, as well as agar plates, should be seeded, and a simultaneous culture should be taken from the arm vein. The author feels that "the same principle can possibly be applied to certain other forms of infections," mentioning osteomyelitis of the leg, for example, as being able to cause a greater blood stream invasion in the corresponding femoral vein. He regards his communication as a preliminary report and hopes that the method may be tried by others, so that "its value, if any, may be determined on a larger amount of material."

RADIOLOGY

UNDER THE CHARGE OF
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Roentgenologic Simulants of Gastric Cancer.—MOORE (*Am. J. Surg.* 1927, **2**, 234) points out that the roentgenologist will seldom overlook a gastric cancer, but he may mistake some other lesion or condition for cancer. Cancer produces a filling defect, which is constant in situation, irregular in outline and sharply delineated; it is not affected by antispasmodics and, if in a region accessible to palpation, a corresponding mass can be felt. Gas in the colon may produce filling defects along the greater curvature; no tumor is palpable and the transparent loop of bowel is readily visible, but the diagnosis of cancer is still made too often in such cases. Deformity of the antrum caused by pressure of the spine is deceptive only if diagnosis is attempted on films alone. Partial hernia of the stomach through the diaphragm gives rise to distortion or hour-glass deformity, which may be attributed to cancer; the barium should be watched as it enters the cardia. Gastrospasm is an annoying simulant of cancer, but the defect is seldom clearly outlined, no corresponding mass can be felt, and, if from causes outside the stomach, usually disappears after belladonna is given. Tumors outside the stomach may indent it, but the rugæ are preserved and peristalsis is not interrupted. Benign tumors tend to produce rounded, central defects. Syphilis imitates cancer in appearance, but seldom gives rise to a palpable tumor, the patient is often under the cancer age and the general condition of the patient is usually good. To avoid errors no diagnosis should be made on films alone, the examination should be roentgenoscopic with thorough manipulation of the stomach and the numerous simulants of cancer should be kept in mind.

Postmortem Roentgenograms in One Hundred Cases of Pulmonary Tuberculosis.—Postmortem roentgenograms were compared with the necropsy findings in 100 cases of pulmonary tuberculosis by HERPEL (*Am. J. Roent. and Rad. Therap.*, 1927, **17**, 436). It was found that 23 per cent of the deaths were due to acute miliary tuberculosis, and the percentage was equally high in young white and young colored males. An astonishing degree of cavitation is compatible with life, and without hemorrhage. Pleuritic adhesions were found with great frequency in all types of the disease. The radiodensity of pleuritis appears to depend largely on the moisture content. Approximately 25 per cent of the patients in this series, who died in an Army hospital, had evidences of combined syphilitic and tuberculous disease. The avoidance of syphilitic and streptococcic infections is of vital importance to tuberculous patients.

Diiodoatophan (Biloptin) in Oral and Duodenal Cholecystography.—Diiodoatophan was first used in cholecystography by Pribram. It contains over 50 per cent of iodin, is a yellowish powder soluble with great difficulty in water or alcohol, is tasteless and when given orally is free from poisonous effects. EINHORN, STEWART and RYAN (*Med. J. and Rec.*, 1927, **125**, 457) have recently tried it in a series of patients both by mouth and through the duodenal tube. For the oral method the biloptin was given in plain gelatin capsules, in a 3-gm. dose with water or milk. Only 1 patient experienced slight nausea. Excellent cholecystograms were obtained twelve to sixteen hours after giving the drug.

The Duodenal Niche.—CARMAN and SUTHERLAND (*Am. J. Roentgenol. and Rad. Ther.*, 1926, **16**, 101) place duodenal ulcer as the most common of all lesions seen roentgenologically in the gastrointestinal tract. The percentage incidence is duodenal ulcer, 56; gastric ulcer, 6; gastric and duodenal ulcer, 1; and gastric cancer 12. Bulbar deformity is the diagnostic anchor. The niche frequently is associated with bulbar deformity, but the greatest value of the niche sign is in the infrequent case in which little or no bulbar deformity is demonstrable. The incidence varies widely with different examiners; Akerlund found it in 50 to 60 per cent; in the Mayo Clinic series 13.27 per cent showed the niche; the difference may be accounted for in the varied conceptions of what constitutes the niche. In the series checked by surgery the diagnosis was remarkably accurate (98 per cent) and there was an element of doubt in the remaining 2 per cent. The niche is an additional sign which offers still greater accuracy in the diagnosis of duodenal ulcer.

The Relative Value of Cholecystography and the So-called Direct and Indirect Methods of Roentgenologic Examination of the Gall Bladder.—CASE (*Am. J. Roentgenol. and Rad. Ther.*, 1926, **16**, 238) prefers the intravenous injection of the dye to the oral administration. The patient eats as usual and comes without any previous preparation. The injection is made about 5 P.M., the patient is kept recumbent for fifteen minutes, an evening meal without fat or protein is allowed, and films are made next morning, fourteen to fifteen hours after the injection. Breakfast, including milk or cream and egg yolk is taken and other films are made at the eighteenth hour. The average patient complains of no discomfort whatever; those who do usually suffer nothing more than a transient malaise. The failure of the gall bladder to acquire enough dye to cast a shadow is the most valuable of all the findings afforded by cholecystography, and no other than the intravenous technique thus far permits dependence upon the reliability of the test. In all cases reported "positive" and "stone positive," surgery is indicated. Slow disappearance of the normal density and faint density with slow emptying suggest chronic catarrhal cholecystitis, but the operative indication in such depends on the history. Reviewing the methods of the "pre-Graham" period, experience with cholecystography has altered some conceptions of the value of indirect signs.

Treatment of Tumors of the Bladder by Deep Roentgen Therapy.—WATERS (*Am. J. Roentgenol. and Radium Ther.*, 1926, **16**, 203) states

that 90 per cent of all vesical neoplasms of epithelial origin are papillary tumors. The other 10 per cent are adenocarcinomas, epithelioma or squamous-cell carcinoma. Excision, as practised, was nearly always followed by recurrence. Fulguration was ideal for benign and malignant papilloma but worse than useless for papillary carcinomas. Superficial papillary carcinoma can be handled successfully by intravesical applications of radium, but deeply or extensively infiltrating tumors and superficial or noninfiltrating papillary carcinomas offer no success by this method. By a combination of fulguration with intravesical applications of radium to the growth through the urethra or destruction of the carcinoma by cautery after suprapubic incision, 75 per cent can be removed. Deep Roentgen ray therapy, with close coöperation of the urologist and roentgenologist affords a relief of root pains and hematuria in inoperable cases that justifies its use.

Toxic Goiter: Treatment by Radium and the Roentgen Rays—STEVENS (*Radiology*, 1927, **8**, 7) believes that radium and the Roentgen rays will probably cure from 66 to 75 per cent of cases of toxic goiter, and that the results are at least equal to those obtained by any other method of treatment. Patients with large tumors, who have symptoms of pressure, ought to be operated on for quick relief. Chronic abscesses or foci of infection should be eradicated in each case of toxic goiter, no matter what treatment is advised.

Surgical Treatment of Cancer.—It would appear, says W. J. MAYO (*Radiology*, 1927, **8**, 93) that uncontrolled oxidation of food, misused for the growth of cells without purpose, is the crime of the neoplastic cell. Kendall has shown that oxidation in the body is influenced by an atom of sulphur in the molecule of the catalyst. It is possible, therefore, that a chemical phase of uncontrolled oxidation in cancer has to do with atomic sulphur. MacCarty's findings would seem to indicate that oxidizing power residues in the nucleolus. Hence any agent such as lead, colloid gold, arsenic, and Coley's serum, which acts as a protoplasmic poison on nucleolar tissue, has an inhibiting effect. That the cell itself is the active agent of cancer is shown by the fact that to develop metastasis the cancer cell must be transplanted. Hence the logic of a direct attack on the cell by the knife, the cautery, electric coagulation, radium and the Roentgen ray. Radium and the Roentgen ray are used so largely in treating inoperable cancer, recurring cancer and metastasis, where only palliation can be expected, that these agents are given too little credit for what they actually accomplish. The work of Erwin Smith, of Slye and of Gye and Barnard suggests that the immunologist will play an important part in the general attack on cancer.

Tabetic Spinal Osteoarthropathy.—Only 60 cases of this disease have been reported. GARVEY and GLASS (*Radiology*, 1927, **8**, 133) add the reports of 4 cases to this number. It occurs independently of trauma to the spine and in spite of antiluetic treatment, comes on late, is found more often in males and may be associated with arthropathy elsewhere.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

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Malignant Hypernephroma Coincident with Arteriosclerosis in Children.—In this article DIETERLE (*J. Nerv. and Ment. Dis.*, 1927, **65**, 42) gives a more complete histopathologic description of Hoag's case of malignant hypernephroma in a child of four years who showed sexual precocity and premature senility. The brain, on examination, showed definite arteriosclerotic changes. He cites the case as evidence of a possible etiologic factor in the production of arteriosclerosis and believes that it is not "unscientific to infer that a hypernephroma, theoretically producing an over abundance of specific secretion, might be the direct factor in producing the arteriosclerotic softening of the brain in this case."

The Malaria Treatment of General Paresis.—FERRARO and FONG (*J. Nerv. and Ment. Dis.*, 1927, **65**, 225) claim that in a series of 120 cases of general paresis treated with malaria, 25.73 per cent showed good remissions, 27.39 per cent marked improvement and 8.3 per cent slight improvement. The total degree of improvement was 61.45 per cent and the death risk only 4.9 per cent. The largest number of good remissions occurred in the expansive-paranoid type. The manic, depressed and expansive-paranoid types offered the highest probability of good remissions following treatment with malaria. The highest number of good and partial remissions occurred between the ages of twenty-six and forty years. Cases of over two years' duration gave fewer remissions than those of eighteen months or less. As against the 53.12 per cent of treated cases showing very good remissions, only 4.8 to 21 per cent of untreated cases showed spontaneous remissions. In 93 cases studied serologically, improvement took place from a minimum of 15 per cent in the first six months to 86 per cent after a period of three years. Sixty-eight per cent of the cases of three years standing showed completely negative spinal Wassermann reactions and the blood Wassermann reaction was negative in 86 per cent of these cases. No absolute parallelism exists between the clinical and the serologic improvement. The neurologic phenomena showing the most marked improvement were the speech defects, coördination tests and tremors. The reflexes seemed to become aggravated in the cases showing partial remissions.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF
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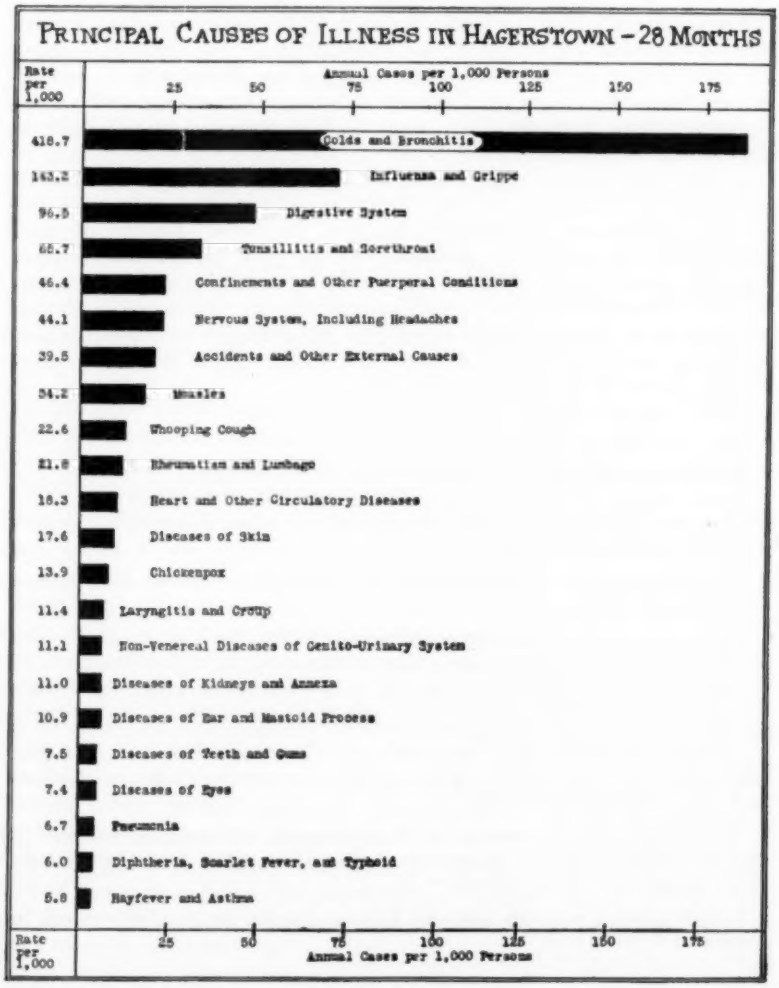
An Epidemic of Glandular Fever (Infectious Mononucleosis).—SPENCER (*U. S. Pub. Health Rep.*, 1926, **41**, 2181) reports on an apparently infectious disease which occurred in a small city in North Carolina in the summer of 1926. The symptoms were as follows: The typical cases were characterized by a few days of general malaise, followed by one or more chills and fever, a general aching all over the body especially severe in the eye muscles and occipital region. Nausea and vomiting and a slight sore throat occurred in about half the cases seen. The fever was usually high at first and gradually tapered off to normal, with an average duration of seven to ten days. In 1 typical case (No. 8) the temperature on the twenty-ninth day was 101° F. in the afternoon. Enlarged tender lymph glands developed in 14 of the 26 cases tabulated below. In some instances the enlarged glands did not develop or were not recognized until late in the illness. Suppuration of the glands did not occur. An unusual feature of the condition was the appearance of a faint but definite rose-colored macular rash over the chest, abdomen, and flexor surfaces of the arms in 13 of the 26 cases. In 1 case (No. 21) the rash was definitely maculopapular and covered the entire body except the face. This case did not show enlarged glands and the patient's blood on the fifteenth day after onset did not agglutinate *B. tularense* or *B. proteus* X_{19}. As a rule, convalescence was prolonged, the patients remaining weak for days. There were no fatalities. There was no significant sex or age grouping. Animal inoculation tests were negative. Epidemiologic surveys and laboratory studies failed to disclose the nature or the mode of transmission. The significant laboratory finding was the large proportion of small lymphocytes running from 43.8 per cent to 84.6 per cent.

Endemic Goiter and School Absenteeism.—OLESEN and TAYLOR (*U. S. Pub. Health Rep.*, 1926, **41**, 2459) say that it has been asserted that goiter as found in the United States has a deleterious influence on the minds and bodies of children. The writers thought this might be reflected in school attendance records. They summarize their studies as follows: Average absences from school were much greater among the colored than among the white children. Among the white children the average absences were slightly greater among the girls. The opposite condition held among the colored children. A comparison of thyroid-normal and thyroid-enlarged children shows, in the particular group under consideration, a slightly greater average absence in the former group. Common colds caused a slightly greater average loss of time from school among the girls. The average time loss of pupils in

the open-air classes exceeded the average absence of those attending the regular classes. Except among the colored boys, the average absence because of common colds was greater among those attending the open-air classes. Absenteeism among the thyroid-normal and thyroid-enlarged children in the open-air classes was irregular in character and without significance, probably because of the small numbers, the lower ages, and relatively small amount of thyroid involvement.

A Study of Illness in a General Population Group.—SYDENSTRICKER (*U. S. Pub. Health Rep.*, 1926, **41**, 2069) reports on an eastern community made up of 93 per cent native whites, 5 per cent of colored, and 2 per cent of foreign born. The number of persons under observation varied from 3202 to 8431, part of the latter being observed for only four months. The principal causes of illness per year per 1000 population was as follows:



Endemic Goiter and Physical Development.—Olesen and Taylor (*U. S. Pub. Health Rep.*, 1926, **41**, 1881) point out that the effects of endemic goiter are not well understood and have been taken for granted rather than demonstrated. It is probable that the impressions with respect to the influence on growth and nutrition have been formed largely by contact with the disease where cretinism, and so forth, are much more frequent than in the United States. The studies on school children by the writers gave the following as the more important of the results: According to the estimates of the examiners, better nutrition and posture were slightly more frequent among thyroid-normal boys and girls. Considerably greater percentages of thyroid-normal children were more than 10 per cent overweight than were thyroid-enlarged individuals. Underweight was more frequent among thyroid-enlarged children. There was little significant difference between the average standing heights of thyroid-normal and thyroid-enlarged boys. The standing heights of thyroid-enlarged girls were greater than those of thyroid-normal girls. Average sitting height was consistently greater among boys and girls with thyroid enlargement. The average weights of thyroid-normal boys and girls were greater than of those having enlarged thyroids. Average chest circumferences, transverse, and antero-posterior chest measurements were slightly greater among children having normal thyroid glands. There were very slight differences in average vital capacities between thyroid-normal and thyroid-enlarged children; the advantage found in this group apparently resting with the former, the greater advantage being with the boys. Despite obvious limitations, the study has apparently shown that children with normal thyroid glands have a definite superiority in certain physical measurements. Consequently it may be assumed that thyroid-normal children are, to some extent, better developed physically. Thyroid-enlarged children, however, appear to have the advantage of slightly greater height, particularly in the sitting position.

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